

REMARKS

Claims 1-20 are pending in the application. Claims 1-15 and 17-20 are cancelled, without prejudice. New Claims 21-25 are added and Claim 16 is amended. Support for new Claims 21-25 can be found, e.g., in originally filed Claim 12. In particular, support for Claim 21 can be found, e.g., on page 18, lines 5-14, and on page 62, lines 33-36. Applicants reserve the right to prosecute the subject matter of Claims 1-11, 19, and 20 in subsequent divisional applications. The Specification is amended to provide a more descriptive title, update the patent family status of the present application, and eliminate browser-executable codes.

Applicants believe no new matter is added by the foregoing amendments.

I. Objections and Informalities

The Examiner objected to the title as not being descriptive of the present invention. Applicants have amended the title accordingly. The Examiner further requested that the patent family status be updated. Applicants have amended the specification to incorporate the proper priority information. The Examiner objected to the Specification for containing browser-executable codes. Applicants have amended the Specification to refer to the websites by a non-executable name.

The Examiner found the present application lacking an abstract. According to the date stamped return receipt postcard (a copy of which accompanies this response), the USPTO received an abstract with the original filing papers. For the Examiner's convenience a copy of the original abstract is enclosed.

In view of the above, Applicants believe that the grounds for these objections have been obviated. Withdrawal of these objections is respectfully requested.

II. Objections to Claims 12 and 16

The Examiner objected to Claims 12 and 16. Claim 12 was objected to as depending from a non-elected claim. Claims 12 and 16 were also objected to as reciting non-elected inventions. Claim 12 is canceled and the objections are therefore moot as to this claim. Claim 16, as amended, no longer recites non-elected inventions. Applicants respectfully request withdrawal of the objections to Claims 12 and 16 in view of the above amendments.

III. Rejection of Claim 12 under 35 U.S.C. 112, Second Paragraph

The Examiner rejected Claim 12 under 35 U.S.C. 112, second paragraph, for indefiniteness. Claim 12 is canceled and the rejection is therefore moot as to this claim. Applicants believe that new Claims 21-25 are free from this rejection.

In view of the above, Applicants respectfully request withdrawal of this rejection.

IV. Rejections of Claims 12-18 under 35 U.S.C. §101

The Examiner rejected Claims 12-18 under 35 U.S.C. §101 alleging that the present invention lacks specific, substantial, and credible utility. Claims 12-15 are canceled and the rejection is therefore moot as to these claims. To satisfy the utility requirement, applications must contain a credible asserted utility that is specific to the subject matter of the invention and involves a "real world" use. Credibility of the asserted substantial and specific utility is judged according to that which "... would be considered credible by the person of ordinary skill in the art" (In re Rinehart 531 F.2d 1048,1052, 189 USPQ 142, 147 (CCPA 1976)).

The Examiner is directed to page 22, lines 6-7, where the Applicants asserted utility for the present cytokine receptor is "... modulation of an inflammatory function ...". This asserted specific and substantial utility is further supported on page 68, lines 29-34, of the specification, where expression of the present invention appears in several in vitro models of the inflammatory state, e.g., activated dendritic cells.

In further support of this asserted utility, Applicants are able to submit extraneous evidence of utility via printed publications as put forth in M.P.E.P 2107.2(VI). Blumberg, et al. (2001) Cell 104:9-19, demonstrates the elevated expression of DIRS1 (a.k.a. IL-20R β) in psoriasis, an inflammatory skin disorder. Blumberg also puts forth evidence receptor signaling when bound by the ligand, IL-20, which is also implicated in various inflammatory skin disorders. Dumoutier, et al. (2001) J. Immunol. 167:3545-3549 further demonstrates that the binding of IL-20 to DIRS1 and another subunit, IL-20R α , results in STAT activation, as well as the implication of the ligand and receptor complex in inflammatory skin disorders.

WO 01/46232, published June 28, 2001, associates the receptor of the present invention, DIRS1 or IL-20R β , with another subunit, IL-20R α , and demonstrates upregulation of the receptor construct psoriasis (see, e.g., page 36, Example 10).

Taken together, Applicants submit that the asserted utility in the present specification is substantial, specific, and credible to the skilled artisan. In view of the above, Applicants respectfully request that the rejection of Claims 12-18 under 35 U.S.C. 101 be withdrawn.

V. Rejection of Claims 12-18 under 35 U.S.C. 112, First Paragraph

The Examiner rejected Claims 12-18 under 35 U.S.C. 112, first paragraph, on the basis that “. . . since the claimed invention is not supported by either a specific and substantial asserted utility . . . one skilled in the art clearly would not know how to use the claimed invention” (Office Action, page 8). Claims 12-15 are canceled and the rejection is therefore moot as to these claims. As noted above, the present invention is supported by a credible, substantial, and specific utility, e.g., modulation of inflammatory responses. Therefore one skilled in the art would, in fact, know how to use the present invention.

The Examiner further alleges that the specification does not enable polypeptide or polynucleotide variants as recited various subsections of Claims 12, 16, and 17, as well as Claims 13-15. Claims 12-15 and 17 are canceled and the rejection is therefore moot as to these claims. The Examiner alleges that the present specification does not provide guidance with regard to the production of fragments having identity to SEQ ID NO:1. As amended Claim 16 does not recite fragments nor do new Claims 21-25.

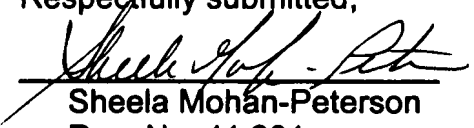
In view of the foregoing, Applicants submit that the rejection of Claims 12-18 is overcome. Withdrawal of this rejection is respectfully requested.

Conclusion

Applicants' current response is believed to be a complete reply to all the outstanding issues of the latest Office Action. Further, the present response is a bona fide effort to place the application in condition for allowance or in better form for appeal. Accordingly, Applicants respectfully request reconsideration and passage of the amended claims to allowance at the earliest possible convenience. Should the Examiner deem allowance inappropriate at this time, Applicants respectfully request an interview be granted with the undersigned to consider any issues.

Date: April 19, 2002

Respectfully submitted,


Sheela Mohan-Peterson
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Attachments:

- (A) Blumberg, et al.
- (B) Dumoutier, et al.
- (C) WO 01/46232
- (D) Copy of Return Receipt Postcard
- (E) Copy of Abstract as filed

(F)

VERSIONS WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph on page 70 (lines 22-27) has been amended as follows:

The cellular forms of receptors for ligands can be tested with the various ligands and receptor subunits provided, e.g., IL-10 related sequences. In particular, multiple cytokine receptor like ligands have been identified, see, e.g., [USN 60/027,368, 08/934,959, and 08/842,659] and U.S. Patent No. 5,989,867 issued to Knappe, et al., which are incorporated herein by reference[.].

The paragraph beginning on page 27 (lines 17-37) and concluding on page 28 (lines 1-9) has been replaced with the following paragraph:

Another example of an algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described Altschul, et al. (1990) J. Mol. Biol. 215:403-410. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information [(http://www.ncbi.nlm.nih.gov/)] on the world wide web at "ncbi.nlm.nih.gov." This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul, et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the

alignment. The BLAST program uses as defaults a wordlength (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Nat'l Acad. Sci. USA 89:10915) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

In the Claims

16. (Amended Once) A nucleic acid which[:
- a)]hybridizes under wash conditions of 30 minutes at [30] 55° C and [less than 2M] 150mM salt to the coding portion of SEQ ID NO: 1[;
 - [b) hybridizes under wash conditions of 30 minutes at 30° C and less than 2M salt to the coding portion of SEQ ID NO: 3; or
 - c) exhibits identity over a stretch of at least about 30 nucleotides to a primate DIRS1; or
 - d) exhibits identity over a stretch of at least about 30 nucleotides to a primate DIRS2].



PubMed	Nucleotide	Protein	Genome	Structure	PopSet	Taxonomy	OMIM	Books
Search: <input type="text" value="Protein"/>		for <input type="text" value=""/>		Go <input type="button" value="Clear"/>				
Limits		Preview/Index		History		Clipboard		Details
Display <input type="button" value="default"/>		Save <input type="button" value="Text"/>		Add to Clipboard <input type="button" value=""/>				

☐ 1: NP_653318. hypothetical prot...[gi:21389499]

 BLink, Nucleotide, Related Sequences, Taxonomy,
LinkOut

LOCUS MGC34923 169 aa linear PRI 11-JUN-2002
 DEFINITION hypothetical protein MGC34923 [Homo sapiens].
 ACCESSION NP_653318
 VERSION NP_653318.1 GI:21389499
 DBSOURCE REFSEQ: accession NM_144717.1
 KEYWORDS .
 SOURCE human.
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 169)
 AUTHORS Strausberg, R.
 TITLE Homo sapiens hypothetical protein MGC34923 (MGC34923), mRNA
 JOURNAL Unpublished (2002)
 COMMENT PREDICTED REFSEQ: The mRNA record is supported by experimental
 evidence; however, the coding sequence is predicted. The reference
 sequence was derived from BC027449.1.
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 121 ysccpvvvp dtlkitnspq kliscreev dacatavmsp eellrawis
 //

Revised: July 5, 2002.

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21389499.1 (1-14)



PubMed	Nucleotide	Protein	Genome	Structure	PopSet	Taxonomy	OMIM	Books
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Limits		Preview/Index		History		Clipboard		Details
Display: <input type="text" value="default"/>		<input checked="" type="checkbox"/> Save		<input type="text" value="Text"/>		<input type="text" value="Add to Clipboard"/>		

☐ 1: NP_653318. hypothetical prot...[gi:21389499]

[BLink](#), [Nucleotide](#), [Related Sequences](#), [Taxonomy](#),
[LinkOut](#)

LOCUS MGC34923 169 aa linear PRI 11-JUN-2002
DEFINITION hypothetical protein MGC34923 [Homo sapiens].
ACCESSION NP_653318
VERSION NP_653318.1 GI:21389499
DBSOURCE REFSEQ: accession [NM_144717.1](#)
KEYWORDS .
SOURCE human.
ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (residues 1 to 169)
AUTHORS Strausberg, R.
TITLE Homo sapiens hypothetical protein MGC34923 (MGC34923), mRNA
JOURNAL Unpublished (2002)
COMMENT PREDICTED REFSEQ: The mRNA record is supported by experimental
evidence; however, the coding sequence is predicted. The reference
sequence was derived from [BC027449.1](#).
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/note="Vector: pCMV-SPORT6"
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121 ysccpvvvlp dtlkitnspq kliscreev dacatavmsp eellrawis
//

Revised: July 5, 2002.

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21389499.1



Conserved Domain Database

PubMed Nucleotide Protein Structure CDD Taxonomy Help?

CD: [pfam01108.5](#), [Tissue fac](#) PSSM-Id: 1658Source: [Pfam\[US\]](#), [Pfam\[UK\]](#)

Description: Tissue factor.

Taxa: [Eutheria](#)References: [1 Pubmed Link](#)

Status: Alignment from source

Created: 13-Jun-2002

Aligned: 5 rows

PSSM: 293 columns Representative: Consensus

Proteins: [\[Click here for CDART summary of Proteins containing pfam01108\]](#)

View Alignment

as

Hypertext

width 60

color at

2.0 bits

Subset Rows

up to 10

of the most diverse members

	10	20	30	40	50	60	
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gi 135666	1	METPAWPRVPRPETAVARTLLLGLWVFAQVAGASGTTNtVAAYNLTWKSTNFKTILEWEPK	60				
gi 135668	1	MAPPTRLQVPRPGTAVPYTVLLGLWLLAQVARAADTTG--RAYNLTWKSTNFKTILEWEPK	58				
gi 401175	1	MATPNGPRVPCPQAARALLFGLVLIQAGVAGTTDvvVAYNITWKSTNFKTILEWEPK	60				
gi 135667	1	MAILVRPRL---LAALAPTFLGCLLLQVIAGAGIPE--KAFNLTWISTDFKTILEWQPK	54				
	70	80	90	100	110	120	
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gi 135666	61	PVNQVYTVQISTKSGDWKSKCFYTTDTECDLTDEIVKDVKQTYLARVFSYPAGN-----	114				
gi 135668	59	SIDHVYTVQISTRLENWKSCKFLTAETECDLTDEVVKDVGQTYMARVLSYPARN-----	112				
gi 401175	61	PINHVYTVQISPRLGWNKNCFYTTTNECDVTDEIVKNVRETYLARVLSYPA-----	112				
gi 135667	55	PTNYTYTVQISDRSRNWNKNCFYTTDTECDLTDEIVKDVTVWAYEAKVLSVPRRNsvhgdg	114				
	130	140	150	160	170	180	
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gi 135666	115	VESTGSAGEPLYENSPEFTPYLETNLQOPTIQSFEQVGTKVNVTVEDERTLVRNNTFLS	174				
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gi 401175	113	-DTSSSTVEPPFTNSPEFTPYLETNLQOPTIQSFEQVGTKLNVTVDARTLVRANSFLS	171				
gi 135667	115	DQLVIHGEEPPFTNAPKFLPYRDTNLGQPVIIQQFEQDGRKLNVVVKDSLTLVRKNGTFLT	174				
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gi 135666	175	LRDVFGKDLIYTLTYWKSSSSGKKTAKTNTNEFLIDVDKGENYCFSVQAVIPSRTVNRKS	234				
gi 135668	173	LRAVFGKDLNYTLYYWRASSTGKKTATTNTNEFLIDVDKGENYCFSVQAVIPSRKRKQRS	232				
gi 401175	172	LRDVFGKDLNYTLYYWKASSTGKKKATTNTNGFLIDVDKGENYCFHVQAVILSRVNQKS	231				
gi 135667	175	LRQVFGKDLGYIITYRKSSTGKKTNIITNTNEFSIDVEEGVSYCFVQAMIFSRKTNQNS	234				
	250	260	270	280	290	300	
consensus	233	PESPTECTSQEKGFLRETFIIGAVVLVVIIFIIIVLSISLHKCRKARAGQSGKENTPLNL	292				
gi 135666	235	TDSPVECMGQEKGEFREIFYIIGAVVFVVIILVILAILSLHKCRKAGVGQSWKENSPLNV	294				
gi 135668	233	PESLTECTSREQGRAREMFFIIGAVV-VVALLIIVLSVTVYKCRKARAGPSGKESSPLNI	291				
gi 401175	232	PESPIKCTSHKVLSTELFFIIGTVMLVIIIFIVVLSVSLHKCRKVRASRGKENTPLNA	291				
gi 135667	235	PGSSTVCTEQWKSFLGETLIIVGAVVLLATIFIILLISLCKRRKNRAGQKQK-NTPSRL	293				

consensus 293 A 293

gi 135666 295 S 295

gi 135668 292 A 292
gi 401175 292 A 292
gi 135667 294 A 294

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NCBI Conserved Domain Search

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RPS-BLAST 2.2.3 [Apr-24-2002]

Query= local sequence:
(311 letters)

Database: oasis_sap.v1.58
4540 PSSMs; 885,521 total columns

Click on boxes for multiple alignments



Domain Relatives

PSSMs producing significant alignments:	Score (bits)	E value
gnl CDD 1658 pfam01108, Tissue_fac, Tissue factor	<u>37.4</u>	7e-04

[gnl|CDD|1658](#), pfam01108, Tissue_fac, Tissue factor.

CD-Length = 293 residues, 85.0% aligned
Score = 37.4 bits (86), Expect = 7e-04

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Sbjct: 19	TLLLGWLLAQVAGAAGTTEKAY-----NLTWKSTNFKTILEWEP--KPINHVVY-TVQIST	70
Query: 73	EYESLYTSHIWIPSSWCSLTEGPECDVTDDITATV--PYNLRVRATLGSQTSAWSILKHP	130
Sbjct: 71	RSGN-----W--KNKCFYTTDTECDLTDEIVKDVQTQYLARVLSYPARNDQTTGSGEPP	122
Query: 131	FNRNS-----TILTRPGME-IXKXGFHLVIELED-----LGPQFE	164
Sbjct: 123	PFTNSPEFTPYLDTNLQPTIQSFEQVGTKLNVTVQDARTLVRRNGTFLSLRDVFGKDLN	182
Query: 165	FLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAYC--VKAQTFVKAIGXYSAFSQTE	222
Sbjct: 183	YTLYYWKASSTGKKTATNTNE----FLIDVDKGENYCFSVQAVIPSRKVNQKSPESPTE	238
Query: 223	CVXV-QGEAIPVLVLAFAFVGFMILILVVV	250
Sbjct: 239	CTSQEKGFLRETFFIIGAVVLVVIIFIIV	267

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results of BLAST

BLASTP 2.2.3 [Apr-24-2002]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1028827051-0733-14680

Query=

(311 letters)

Database: All non-redundant GenBank CDS

translations+PDB+SwissProt+PIR+PRF

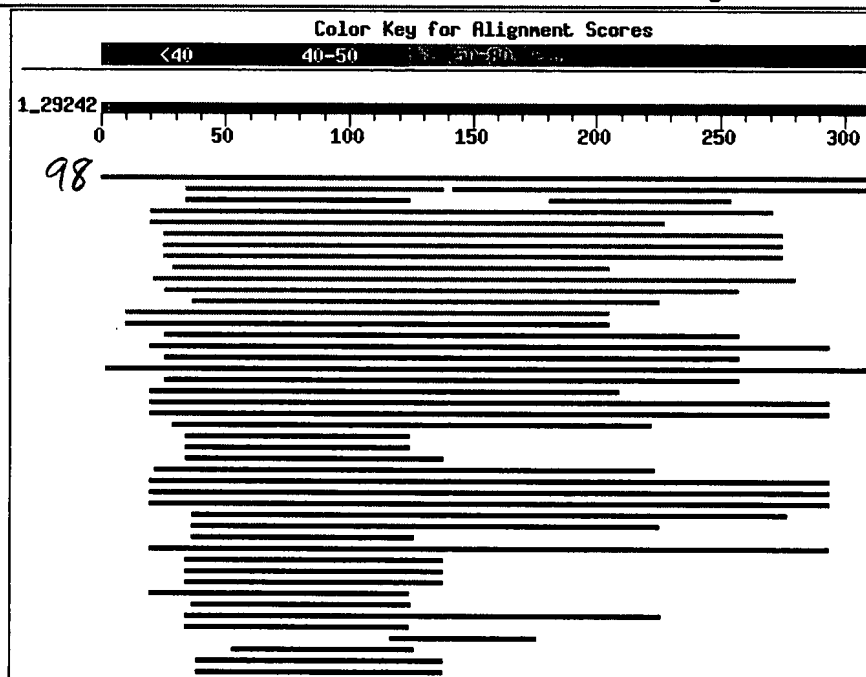
1,047,264 sequences; 330,262,426 total letters

If you have any problems or questions with the results of this search please refer to the [BLAST FAQs](#)

[Taxonomy reports](#)

Distribution of 50 Blast Hits on the Query Sequence

Mouse-over to show defline and scores. Click to show alignments



Sequences producing significant alignments:

Score E
(bits) Value

gi 20536050 ref XP_087367.2	(XM_087367) similar to interle...	597	e-170	
gi 21389499 ref NP_653318.1	(NM_144717) hypothetical prote...	323	2e-87	L
gi 20893710 ref XP_135077.1	(XM_135077) hypothetical prote...	77	2e-13	L
gi 4028135 gb AAD13669.1	(AF082664) interferon alpha/beta ...	69	1e-10	
gi 4028143 gb AAD13679.1	(AF082667) interferon alpha/beta ...	61	1e-08	
gi 20560916 ref XP_114185.1	(XM_114185) interleukin 10 rec...	59	6e-08	
gi 19923113 ref NP_000619.2	(NM_000628) interleukin 10 rec...	59	6e-08	L
gi 7512371 pir G01418	cytokine receptor family II, member ...	58	1e-07	
gi 18593097 ref XP_048563.2	(XM_048563) interferon gamma r...	54	2e-06	
gi 4028139 gb AAD13671.1	(AF082666) interleukin-10 recepto...	52	1e-05	
gi 7513699 pir JC6311	interferon receptor-class II cytokin...	51	2e-05	
gi 17105372 ref NP_476541.1	(NM_057193) interleukin 10 rec...	51	2e-05	L
gi 15212826 gb AAK85714.1	(AY040566) interleukin 22-bindin...	51	2e-05	L
gi 463552 gb AAA16956.1	(U05877) AF-1 [Homo sapiens] >gi 1...	50	3e-05	L
gi 5031783 ref NP_005525.1	(NM_005534) interferon gamma re...	50	4e-05	L
gi 6680391 ref NP_032375.1	(NM_008349) interleukin 10 rece...	50	5e-05	L
gi 17646388 gb AAL40946.1	AF440787_1 (AF440787) interleukin...	49	5e-05	L
gi 462415 sp Q04790 INR1 BOVIN	INTERFERON-ALPHA/BETA RECEPT...	49	6e-05	
gi 6754302 ref NP_034638.1	(NM_010508) interferon (alpha a...	48	2e-04	L
gi 20896187 ref XP_128323.1	(XM_128323) similar to interle...	47	2e-04	L
gi 163188 gb AAA02571.1	(L06320) alpha-interferon receptor...	47	4e-04	
gi 2612835 gb AAB84231.1	(U65978) interferon alpha/beta re...	46	4e-04	
gi 2494729 sp Q28589 INR1 SHEEP	INTERFERON-ALPHA/BETA RECEPT...	46	4e-04	
gi 6680373 ref NP_032364.1	(NM_008338) interferon gamma re...	46	5e-04	L
gi 7657691 ref NP_055247.1	(NM_014432) interleukin 20 rece...	46	6e-04	L
gi 12732140 ref XP_004438.2	(XM_004438) interleukin 20 rec...	46	6e-04	L
gi 14031070 emb CAC38376.1	(AL135902) bA204P2.1.3 (interle...	45	9e-04	
gi 6680389 ref NP_032374.1	(NM_008348) interleukin 10 rece...	45	0.001	L
gi 20856437 ref XP_136952.1	(XM_136952) similar to bA204P2...	44	0.002	L
gi 10835183 ref NP_000620.1	(NM_000629) interferon (alpha,...	43	0.005	L
gi 16166194 ref XP_048562.2	(XM_048562) similar to interfe...	43	0.005	L
gi 32672 emb CAA42992.1	(X60459) interferon alpha/beta rec...	43	0.005	L
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gi 4028141 gb AAD13677.1	(AF082667) interferon alpha/beta ...	42	0.010	
gi 16418459 ref NP_443194.1	(NM_052962) class II cytokine ...	42	0.011	L
gi 15988304 pdb 1J7V R	Chain R, Human IL-10 IL-10r1 Complex	41	0.019	
gi 106794 pir S17112	interferon alpha/beta receptor - human	41	0.021	
gi 4504633 ref NP_001549.1	(NM_001558) interleukin 10 rece...	40	0.036	L
gi 20560751 ref XP_006447.7	(XM_006447) similar to Interle...	40	0.036	L
gi 11991877 gb AAG42376.1	AF296666_1 (AF296666) type I inte...	40	0.044	
gi 15212830 gb AAK85716.1	(AY040568) interleukin 22-bindin...	39	0.087	L
gi 20896935 ref XP_139651.1	(XM_139651) similar to INTERFE...	35	0.80	L
gi 18547428 ref XP_089078.1	(XM_089078) similar to interle...	35	0.85	L
gi 15602147 ref NP_245219.1	(NC_002663) unknown [Pasteurel...	33	3.6	
gi 2129405 pir S53867	DNA (cytosine)-methyltransferase (EC...	33	4.6	
gi 3980170 emb CAA37597.1	(X53521) brain tissue factor [Or...	32	6.8	
gi 3212253 pdb 1A21 B	Chain B, Tissue Factor (Tf) From Rabb...	32	7.0	

Alignments

>gi|20536050|ref|XP_087367.2| (XM_087367) similar to interleukin 10 receptor, beta
 receptor family II, member 4; human transmembrane
 receptor protein; cytokine receptor [Homo sapiens]
 Length = 311

Score = 597 bits (1539), Expect = e-170

Identities = 306/311 (98%), Positives = 306/311 (98%)

Query: 1 MQFTTMVLEEIIWTSFLMFWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAP 60
 MQFTTMVLEEIIWTSFLMFWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAP
 Sbjct: 1 MQFTTMVLEEIIWTSFLMFWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAP 60

Query: 61 GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120
 GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ
 Sbjct: 61 GETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120

Query: 121 TSAWSILKHPFNRNSTILTRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEHV 180
 TSAWSILKHPFNRNSTILTRPGMEI K GFHLVIELEDLGPQFEFLVAYW REPGAEHV
 Sbjct: 121 TSAWSILKHPFNRNSTILTRPGMEITKDGHLVIELEDLGPQFEFLVAYWRREPGAEHV 180

Query: 181 KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTCEVXVQGEAIPLVLALFAF 240
 KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIG YSAFSQTECV VQGEAIPLVLALFAF
 Sbjct: 181 KMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTCEVEVQGEAIPLVLALFAF 240

Query: 241 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM 300
 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM
 Sbjct: 241 VGFMLILVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVM 300

Query: 301 SPEELLRAWIS 311
 SPEELLRAWIS
 Sbjct: 301 SPEELLRAWIS 311

>gi|21389499|ref|NP_653318.1| **L** (NM_144717) hypothetical protein MGC34923 [Homo sap
 gi|20072749|gb|AAH27449.1| **L** (BC027449) similar to interferon alpha/beta receptor
 sapiens]
 Length = 169

Score = 323 bits (827), Expect = 2e-87
 Identities = 164/169 (97%), Positives = 164/169 (97%)

Query: 143 MEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEHV KMVRSGGIPVHLETMEPGAAYC 202
 MEI K GFHLVIELEDLGPQFEFLVAYW REPGAEHV KMVRSGGIPVHLETMEPGAAYC
 Sbjct: 1 MEITKDGHLVIELEDLGPQFEFLVAYWRREPGAEHV KMVRSGGIPVHLETMEPGAAYC 60

Query: 203 VKAQTFVKAIGXYSAFSQTCEVXVQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ 262
 VKAQTFVKAIG YSAFSQTECV VQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ
 Sbjct: 61 VKAQTFVKAIGRYSAFSQTCEVEVQGEAIPLVLALFAFVGFMLILVVVPLFVWKMGRLLQ 120

Query: 263 YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS 311
 YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS
 Sbjct: 121 YSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS 169

>gi|20893710|ref|XP_135077.1| **L** (XM_135077) hypothetical protein XP_135077 [Mus mus
 Length = 112

Score = 77.4 bits (189), Expect = 2e-13
 Identities = 44/74 (59%), Positives = 48/74 (64%), Gaps = 7/74 (9%)

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTCEVXVQGEAIPLVLALFAFV 241
 MVRSG IPVHLETMEPGA YCVKAQ VKAIG +SAFSQ CV +QG+ LV
 Sbjct: 1 MVRSGDIPVHLETMEPGAMYCVKAQALVKAIGRHSAFSQPTCVEMQKDNLLVPG----- 55

Query: 242 GFMLILVVVPLFVW 255
 L L +PL W
 Sbjct: 56 --SLHLAALPLHAW 67

>gi|4028135|gb|AAD13669.1| (AF082664) interferon alpha/beta receptor 1 [Gallus gal
 Length = 569

Score = 68.6 bits (166), Expect = 1e-10
 Identities = 73/273 (26%), Positives = 117/273 (42%), Gaps = 25/273 (9%)

Query: 21 YALIPCL-LTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEY-QGEYESLY 78
 ++ I C+ T +V L P N+ V + NMK L+W E V Y+V+Y G ++LY
 Sbjct: 222 FSPIHCICKTRKVNLLCPTNVRVFAFNMKFYLLWDNHY--NEHVITYTVQYLTGYLKNLY 279

Query: 79 T--SHIWIPSSWCSLTEGPECDVTDDITAT-VPYNLRVRATLGSQTSAWS--ILKHFPNR 133
 S W S C +C+++ I T Y RV+A S S + P
 Sbjct: 280 DDYSSKWQKVSGCENITSMKCNLSSVIKPTSASYFRVQAMNEYSKSLSKDVEVDPPVT 339

Query: 134 NSTILTRPGMEIXKXGFHLVIE-----LEDLGPQFEFLVAYWXREPAAEEHVKMVR 184
 N ++I H+ I + DL F + + YW EE VKM
 Sbjct: 340 NEIGPPDVKVDISDVLLHIKITPPGGPGNKIMSDL-YDFSQILYWKNSDNEEEVKMKE 398

Query: 185 SGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQ-GEAIPVLALFAFVGF 243
 + + + P YCVK Q F +A S FS+ EC+ G+ +PL++ L F G
 Sbjct: 399 TKQTIATVSDLAPSTLYCVKQAFSEAYNKSSDFSREECIGTAGGKHLPLII-LATFAGA 457

Query: 244 MLILVVVP----LFVWKMGRLLQYSCCPVVVLP 272
 + ++++V F++++ ++Y P P
 Sbjct: 458 LTVVLIVASLVIFFLYQVYNKIKYMFPPSCQTP 490

Score = 47.4 bits (111), Expect = 2e-04

Identities = 53/206 (25%), Positives = 82/206 (39%), Gaps = 25/206 (12%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTE 93
 L +PQ++ V + N LMW+ G V +S +YQ ++ L TS W S C
 Sbjct: 32 LKSPQDIQVYAVNTNFTLMWN-YTGDGTNVTFSAQYQC-FDDLQTSEPEWKELSGCQNV 89

Query: 94 GPECDVTDDITATV-PYNLRVRATLGSQTSAWSILKHFPNRNSTILTRPGMEIXKXGFHL 152
 ECD + ITA ++R+RA S WS + + P EI +
 Sbjct: 90 HTECDFSSAITAYDTHHIRAERREAKSPWSSIFEMIPYEIAQIGPP--EIALQSING 147

Query: 153 VIELEDLGPQ-----FEFLVAYWXREPAAEEHVKMVRSGGIPVH-LETMEPG 198
 I++ P+ F++ V W E+ VRS +P+ + + P
 Sbjct: 148 AIKINISPPEANQVRKMWLISVFFKYNVVIWDNSSNVEK----VRS-ILPIDVINDLAPE 202

Query: 199 AAYCVKAQTFVKAIGXYSAFSQTECV 224
 YC+K Q V FS C+
 Sbjct: 203 TTYCLKVQATVPLEDKGGLFSPIHCI 228

>gi|4028143|gb|AAD13679.1| (AF082667) interferon alpha/beta receptor 1 [Gallus gal
 Length = 442

Score = 61.2 bits (147), Expect = 1e-08

Identities = 63/224 (28%), Positives = 92/224 (40%), Gaps = 19/224 (8%)

Query: 21 YALIPCL-LTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEY-QGEYESLY 78
 ++ I C+ T +V L P N+ V + NMK L+W E V Y+V+Y G ++LY
 Sbjct: 222 FSPIHCIKTTRKVNLLCPTNVRVFALNMKFYLLWDNHY--NEHVITYTVQYLTYGLKNLY 279

Query: 79 T--SHIWIPSSWCSLTEGPECDVTDDITAT-VPYNLRVRATLGSQTSAWS--ILKHFPNR 133
 S W S C +C+++ I T Y RV+A S S + P
 Sbjct: 280 DDYSSKWQKVSGCENITSMKCNLSSVIKPTSASYFRVQAMNEYSKSLSKDVEVDPPVT 339

Query: 134 NSTILTRPGMEIXKXGFHLVIE-----LEDLGPQFEFLVAYWXREPAAEEHVKMVR 184
 N ++I H+ I + DL F + + YW EE VKM
 Sbjct: 340 NEIGPPDVKVDISDVLLHIKITPPGGPGNKIMSDL-YDFSQILYWKNSDNEEEVKMKE 398

Query: 185 SGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQ 228
 + + + P YCVK Q F +A S FS+ EC+ G
 Sbjct: 399 TKQTIATVSDLAPSTLYCVKQAFSEAYNKSSDFSREECIGTAG 442

Score = 47.8 bits (112), Expect = 2e-04

Identities = 53/206 (25%), Positives = 82/206 (39%), Gaps = 25/206 (12%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTE 93
 L +PQ++ V + N LMW+ G V +S +YQ ++ L TS W S C
 Sbjct: 32 LKSPQDIQVYAVNTNFTLMWN-YTGDGTNVTFSAQYQC-FDDLQTSEPEWKELSGCQNV 89

Query: 94 GPECDVTDDITATV-PYNLRVRATLGSQTSASWILKHPFNRNSTILTRPGMEIXKXGFHL 152
 ECD + ITA +++R+RA S WS + + P EI +
 Sbjct: 90 HTECDFSSAITAYDTHHIRIRAERREAKSPWSSIFEMIPYEIAQIGPP--EIALQSING 147

Query: 153 VIELEDLGPQ-----FEFLVAYWXREPGAEHVKMVRSGGIPVH-LETMEPG 198
 I++ P+ F++ V W E+ VRS +P+ + + P
 Sbjct: 148 AIKINISPPEANQVRKMWLISVFFKYNVVIWDNSSNVEK----VRS-ILPIDVINDLAPE 202

Query: 199 AAYCVKAQTFVKAIGXYSAFSQTECV 224
 YC+K Q V FS C+
 Sbjct: 203 TTYCLKVQATVPLEDKGLFSPHICI 228

>gi|20560916|ref|XP_114185.1| (XM_114185) interleukin 10 receptor, beta [Homo sapiens]
 gi|12804903|gb|AAH01903.1|AAH01903 (BC001903) Similar to interleukin 10 receptor,
 Length = 325

Score = 59.3 bits (142), Expect = 6e-08
 Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26 CLLTDEVAILPAPQNLSVLSTNMKHLMLW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84
 CLL + ++P P+N+ + S N K++L W SP A G ++ + +Y S I
 Sbjct: 12 CLLVSALGMVPPPENVRMNSVNFKNILQWESPFAK-----NLTFTAQYLSYR-----I 61

Query: 85 PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSASW-SILKHPFNRNSTILTRPGM 143
 C T ECD + ++ + LRVRA + S W +I P + TI+ PGM
 Sbjct: 62 FQDKCMNTTLTECDFSS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144 --EIXKXGFHLVIELEDLGPQFE-----FLVAYWXREPGAEHVKMVRSGGIP 189
 E+ H+ + ++E + V YW + G +E ++
 Sbjct: 119 QVEVLADSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190 VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAFVGFMFI 246
 V L +EP YCV+ + F+ +S+ C E +P +V + FM+
 Sbjct: 177 V-LRNLEPWTTCVQVRGFLPDRNKAGEWSEPVEQTTTHDETVPSSWMVAVILMASVFMVC 235

Query: 247 LVVVPLF--VWKMGRLQLYSCCPVVVLPDTLK 276
 L ++ F +W + + +Y+ P LP LK
 Sbjct: 236 LALLGCFALLWCYKTKYAFSPRNSLPQHLK 267

>gi|19923113|ref|NP_000619.2| **L** (NM_000628) interleukin 10 receptor, beta; cytokine
 II, member 4; human transmembrane receptor protein;
 cytokine receptor [Homo sapiens]
 gi|729209|sp|Q08334|I10S HUMAN Interleukin-10 receptor beta chain precursor (IL-1
 Cytokine receptor class-II CRF2-4)
 gi|627419|pir|A47003 cytokine receptor family class II protein CRF2-4 precursor
 gi|393379|emb|CAA78933.1| **L** (Z17227) transmembrane receptor precursor [Homo sapiens]
 Length = 325

Score = 59.3 bits (142), Expect = 6e-08
 Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26 CLLTDEVAILPAPQNLSVLSTNMKHLMLW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84
 CLL + ++P P+N+ + S N K++L W SP A G ++ + +Y S I
 Sbjct: 12 CLLVSALGMVPPPENVRMNSVNFKNILQWESPFAK-----NLTFTAQYLSYR-----I 61

Query: 85 PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSASW-SILKHPFNRNSTILTRPGM 143
 C T ECD + ++ + LRVRA + S W +I P + TI+ PGM
 Sbjct: 62 FQDKCMNTTLTECDFSS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144 --EIXKXGFHLVIELEDLGPQFE-----FLVAYWXREPGAEHVKMVRSGGIP 189
 E+ H+ + ++E + V YW + G +E ++
 Sbjct: 119 QVEVLADSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190 VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAFVGFMFI 246

V L +EP YCV+ + F+ +S+ C E +P +V + FM+
 Sbjct: 177 V-LRNLEPWTTCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMMVAVILMASVFMVC 235

Query: 247 LVVVPLF--VWKMGRLLQYSCCPVVLPDTLK 276

L ++ F +W + + +Y+ P LP LK

Sbjct: 236 LALLGCFSLLWCYKKTGYAFSPRNSLPQHLK 267

>gi|7512371|pir|G01418 cytokine receptor family II, member 4 - human
 gi|571296|gb|AAA86872.1| L (U08988) CRFB4 [Homo sapiens]
 Length = 273

Score = 58.2 bits (139), Expect = 1e-07

Identities = 69/272 (25%), Positives = 116/272 (42%), Gaps = 37/272 (13%)

Query: 26 CLLTDEVAILPAPQNLSVLSTNMKHLMLW-SPVIAPGETVYYSVEYQGEYESLYTSHIWI 84

CLL + ++P P+N+ + S N K++L W SP A G ++ + +Y S I

Sbjct: 12 CLLVSALGMVPPPENVRMNSVNFKNILQWESPAFAKG-----NLTFTAQYLSYR-----I 61

Query: 85 PSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSW-SILKHPFNRNSTILTRPGM 143

C T ECD + ++ + LRVRA + S W +I P + TI+ PGM

Sbjct: 62 FQDKCMNTTLTECDFS-SLSKYGDHTLRVRAEFADEHSDWVNITFCPV--DDTIIGPPGM 118

Query: 144 --EIXKXGFHLVIELEDLGPQFE-----FLVAYWXREPGAEEHVKMVRSGGIP 189

E+ H+ + ++E + V YW + G +E ++

Sbjct: 119 QVEVLDDSLHMRFLAPKIENEYETWTMKNVYNSWTYNVQYW--KNGTDEKFQITPQYDFE 176

Query: 190 VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTEC-VXVQGEAIP--LVLALFAVGFMLI 246

V L +EP YCV+ + F+ +S+ C E +P +V + FM+

Sbjct: 177 V-LRNLEPWTTCVQVRGFLPDRNKAGEWSEPVCEQTTHDETVPSWMMVAVILMASVFMVC 235

Query: 247 LVVVPLF--VWKMGRLLQYSCCPVVLPDTLK 276

L ++ F +W + + +Y+ P LP LK

Sbjct: 236 LALLGCFSLLWCYKKTGYAFSPRNSLPQHLK 267

>gi|18593097|ref|XP_048563.2| (XM_048563) interferon gamma receptor accessory fact
 sapiens]
 Length = 356

Score = 53.9 bits (128), Expect = 2e-06

Identities = 56/193 (29%), Positives = 85/193 (44%), Gaps = 20/193 (10%)

Query: 30 DEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGET--VYYSVEYQGEYESLYTSHIWI 87

D ++ LPAPQ+ + N + +L W PV T V Y V+++ +T+ I

Sbjct: 44 DPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYQVQFKYTDSKWFTADIMSIGV 103

Query: 88 WCSLTEGPECDVT-DDITATVPYN---LRVRATLGSQTSW-SILK-HPFNRNSTILTRP 141

C+ ECD T +A P + LR+RA LG+ SAW + RN T+

Sbjct: 104 NCTQITATECDFTAASPSAGFPMDFNVTLRLRAELGALHSAWVTMPWFQHYRNVTVGPPE 163

Query: 142 GMEIXKXGFHLVIELE---DLGPQ---FEFLVAYWXREPGAEEHVK-MVRSGGIPVHLE 193

+E+ L+I D+ F + V YW E G + VK RS I L+

Sbjct: 164 NIEVTPGEGSLIIRFSSPFDIADTSTAFFCYVHYW--EKGGIQQVKGPFRSNSIS--LD 219

Query: 194 TMEPGAAYCVKAQ 206

++P YC++ Q

Sbjct: 220 NLKPSRVYCLQVQ 232

>gi|4028139|gb|AAD13671.1| (AF082666) interleukin-10 receptor 2 [Gallus gallus]
 gi|4028142|gb|AAD13678.1| (AF082667) interleukin-10 receptor 2 [Gallus gallus]
 Length = 341

Score = 51.6 bits (122), Expect = 1e-05

Identities = 59/279 (21%), Positives = 115/279 (41%), Gaps = 29/279 (10%)

Query: 22 ALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSH 81

AL CLL I+P P+N + S N + +L+W P + Y+V+ + + ++
 Sbjct: 8 ALWGCLLLCVSGIVPKPRNARISSVNFERSVLLWDPGVRKGNLSYTVQAKSIFPKQNFNN 67

Query: 82 IWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILTRP 141
 + ++ ++T ECDV+ ++ Y LRVR + S W++++ T++ P
 Sbjct: 68 V---TTNLNVT---ECDVS-SLSVYGAYVLRVRTEWEDEHSDWAVVRFK-PMADTVIGPP 119

Query: 142 GMEIXKXGFHLVIELEDLGPQFE-----FLVAYWXREPAAEEHVKMVRSGG 187
 + + L ++ E + + YW + G + V + +
 Sbjct: 120 SVNKSESGLTHVDFTGPAADREHDKWSLKQYYGSIYRILYWKK--GSNKKVIHIDTKH 177

Query: 188 IPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAI-PLVLALFAFVGFMIL- 245
 L +EP YC++ Q + SQ C + P+ + + +G ML
 Sbjct: 178 NSEILSQLEPWTIYCIQVQGVPEWNKTGERSQELCEQTTHNGVTPVWIVVTVLLGSMIL 237

Query: 246 ILVVVPL---FVWKMGRLLQYSCCPVVVLPDTLKITNSP 281
 +++ VP+ W + R ++ P + P LK SP
 Sbjct: 238 VIISVPVCFFAFWYLYRFTKHVFFPSYIFPQHLKEFFSP 276

>gi|7513699|pir||JC6311 interferon receptor-class II cytokine receptor - mouse
 Length = 349

Score = 51.2 bits (121), Expect = 2e-05
 Identities = 61/249 (24%), Positives = 103/249 (40%), Gaps = 38/249 (15%)

Query: 27 LLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
 LL + ++P P+ + + S N K++L W P + ++ +Y+ Y S + H
 Sbjct: 13 LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAFPKTNLTFTAQYE-SYRS-FQDH----- 65

Query: 87 SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSASW-SILKHPFNRNSTILTRPGMEI 145
 C T +CD + ++ Y +RVRA L + S W ++ P TI+ P M+I
 Sbjct: 66 --CKRTASTQCDFS-HLSKYGDYTVRVRRAELADEHSEWVNVTFPCV--EDTIIGPPEMQI 120

Query: 146 KXKXGFHLVIELEDLGPQFE-----FLVAYWXREPAAEEHVKMVRSGGIP 189
 L EL PQ E + V YW + G E ++V
 Sbjct: 121 ESLAESL--ELRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSYPYDSE 176

Query: 190 VHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPLVLALFAFVGFMILILVV 249
 V L +EP YC++ Q F+ +S+ C + I V +LI+ V
 Sbjct: 177 V-LRNLEPWTIYCIQVQGFLLDQNRGTGEWSEPICERTGNDEITPSW----IVAILIVSV 231

Query: 250 VPLFVWKMG 258
 + +F++ +G
 Sbjct: 232 LVVFLFLLG 240

>gi|17105372|ref|NP_476541.1| (NM_057193) interleukin 10 receptor, alpha [Rattus
 gi|12330005|emb|CAC24567.1| (AJ305049) interleukin-10 receptor, alpha chain [Rat
 Length = 569

Score = 50.8 bits (120), Expect = 2e-05
 Identities = 33/108 (30%), Positives = 50/108 (45%), Gaps = 8/108 (7%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
 LP+P ++ + +H+L W + E+ YY V + Y + IW CS +
 Sbjct: 26 LPSPSSVWFEARFFQHILRWMSIPNQSESTYYEVALKK-----YGTSIWKDIHICSKAQT 80

Query: 95 PECDVTD---DITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
 CD+T D+ + Y RVRA SQ S W+I + F + ILT
 Sbjct: 81 LSCDLTTSTLDLYHSSGYRARVRVDNSQYSNWTITETRTVDEVILT 128

>gi|15212826|gb|AAK85714.1| (AY040566) interleukin 22-binding protein CRF2-10 [Ho
 gi|15419023|gb|AAK91775.1| (AY044429) class II cytokine receptor [Homo sapiens]
 gi|16304591|emb|CAC85634.1| (AJ313161) soluble cytokine class II receptor, short
 sapiens]

gi|17974197|emb|CAC83097.1| (AJ297262) interleukin-22 binding protein [Homo sapiens]
Length = 231

Score = 50.8 bits (120), Expect = 2e-05
Identities = 49/205 (23%), Positives = 79/205 (37%), Gaps = 21/205 (10%)

Query: 38 PQNLSVLSTNMKHLWMSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPE 96
PQ + S N ++L W P A G + Y V+Y+ +Y W C T+
Sbjct: 31 PQRVQFQSRNFHNLQWQPGRALTGNSSVYFVQYK-----IYGQRQWKNKEDCWGTQELS 85

Query: 97 CDVTDDIT-ATVPYNLRVRATLGSQTSASILKHPFNRNSTILTRPGMEIXKXGFHLVIE 155
CD+T + + PY RVRA S WS+ T + P M I + L++
Sbjct: 86 CDLTSETSDIQEPYGRVRAASAGSYSEWSMTPRFTPPWETKIDPPVMNITQVNGSLLVI 145

Query: 156 LE-----DLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVHLETMEPGAAY 201
L + +E L + E+ K+ V +E + P ++Y
Sbjct: 146 LHAPNLPYRYQKEKNVSIEDYYELLYRVFIINNSLEKEQKVYEGAHRAVEIEALTPHSSY 205

Query: 202 CVKAQTFVKAIGXYSAFSQTECVXV 226
CV A+ + + S S+ CV +
Sbjct: 206 CVVAEIQPMLDRRSQRSEERCVEI 230

>gi|463552|gb|AAA16956.1| (U05877) AF-1 [Homo sapiens]
gi|13177682|gb|AAH03624.1|AAH03624 (BC003624) interferon gamma receptor 2 (interferon gamma receptor 2) [Homo sapiens]
Length = 337

Score = 50.1 bits (118), Expect = 3e-05
Identities = 59/212 (27%), Positives = 92/212 (42%), Gaps = 20/212 (9%)

Query: 11 IWTSLFMWFFYALIPCLLTDEVAAILPAPQNLSVLSTNMKHLWMSPVIA-PGET--VYYSV 68
+W+ L + +A D ++ LPAPQ+ + N + +L W PV T V Y V
Sbjct: 6 LWSLLLLLLGVFAAAAAAPPDPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYQV 65

Query: 69 EYQGEYESLYTSHIWIPSSWCSLTEGPECDVT-DDITATVPYN----LRVRATLGSQTS 123
+++ +T+ I C+ ECD T +A P + LR+RA LG+ SA
Sbjct: 66 QFKYTDSKWFTADIMSIGVNCTQITATECDFTAASPSAGFPMDFNVTLLRLRAELGALHSA 125

Query: 124 WSILK-HPFNRNSTILTRPGMEIXKXGFHLVIELE---DLGPQ----FEFLVAYWXREPG 175
W + RN T+ +E+ L+I D+ F + V YW E G
Sbjct: 126 WVTMPWFQHYRNVTVGPPENIEVTPGEGSLIIRFSSPFDIADTSTAFFCYVHYW--EKG 183

Query: 176 AEEHVK-MVRSGGIPVHLETMEPGAAYCVKAQ 206
+ VK RS I L+ ++P YC++ Q
Sbjct: 184 GIQQVKGPFRSNSIS--LDNLKPSRVYCLQVQ 213

>gi|5031783|ref|NP_005525.1| (NM_005534) interferon gamma receptor 2 (interferon gamma receptor 2) [Homo sapiens]
transducer 1); interferon gamma receptor accessory factor-1; interferon-gamma receptor beta chain precursor
gi|585319|sp|P38484|INGH HUMAN Interferon-gamma receptor beta chain precursor (Interferon-gamma receptor accessory factor-1) (AF-1) (Interferon-gamma receptor accessory factor-1) [Homo sapiens]
gi|2135504|pir|I38500 interferon gamma receptor accessory factor-1 precursor - h
gi|463550|gb|AAA16955.1| (U05875) AF-1 [Homo sapiens]
Length = 337

Score = 49.7 bits (117), Expect = 4e-05
Identities = 59/212 (27%), Positives = 92/212 (42%), Gaps = 20/212 (9%)

Query: 11 IWTSLFMWFFYALIPCLLTDEVAAILPAPQNLSVLSTNMKHLWMSPVIA-PGET--VYYSV 68
+W+ L + +A D ++ LPAPQ+ + N + +L W PV T V Y V
Sbjct: 6 LWSLLLLLLGVFAAAAAAPPDPLSQLPAPQHPKIRLYNAEQVLSWEPVALSNSTRPVVYRV 65

Query: 69 EYQGEYESLYTSHIWIPSSWCSLTEGPECDVT-DDITATVPYN----LRVRATLGSQTS 123

+++ +T+ I C+ ECD T +A P + LR+RA LG+ SA
 Sbjct: 66 QFKYTD SKWFTADIMSIGVNCTQITATECDFTAASPSAGFPMDFNVTLRLRAELGALHSA 125
 Query: 124 WSILK-HPFNRNSTILTRPGMEIXKXGFHLVIELE---DLGPQ----FEFLVAYWXREPG 175
 W + RN T+ +E+ L+I D+ F + V YW E G
 Sbjct: 126 WVTMPWFQHYRNVTVGPPENIEVTPGEGSLIIRFSSPFDIADTSTAFFCYVHYW--EKG 183

Query: 176 AEEHVK-MVRSGGIPVHLETMEPGAAYCVKAQ 206
 + VK RS I L+ ++P YC++ Q
 Sbjct: 184 GIQQVKGPFRSNSIS--LDNLKPSRVYCLQVQ 213

>gi|6680391|ref|NP_032375.1| (NM_008349) interleukin 10 receptor, beta [Mus muscu
 gi|10720037|sp|Q61190|I10S MOUSE Interleukin-10 receptor beta chain precursor (IL
 (Cytokine receptor class-II CRF2-4)
 gi|1305489|gb|AAC53062.1| (U53696) class II cytokine receptor 4 [Mus musculus].
 Length = 349

Score = 49.7 bits (117), Expect = 5e-05
 Identities = 57/247 (23%), Positives = 104/247 (42%), Gaps = 34/247 (13%)

Query: 27 LLTDEVAILPAPQNLSVLSTNMKHLWMSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
 LL + ++P P+ + + S N K++L W P + ++ +Y+ Y S + H
 Sbjct: 13 LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAPKTNLTFTAQYE-SYRS-FQDH----- 65
 Query: 87 SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTS AW-SILKHPFNRNSTILTRPGMEI 145
 C T +CD + ++ Y +RVRA L + S W ++ P TI+ P M+I
 Sbjct: 66 --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFPCV--EDTIIGPPEMQI 120

Query: 146 KXXGFHLVIE-----LEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVH 191
 L + L+++ + + V YW + G E ++V V
 Sbjct: 121 ESLAESLHLRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVS PYDSEV- 177

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPVLALFAFVGFM LILVVVP 251
 L +EP YC++ Q F+ +S+ C + I V +LI+ V+
 Sbjct: 178 LRNLEPWTTCYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAILIVSVLV 233

Query: 252 LFWVKMG 258
 +F++ +G
 Sbjct: 234 VFLFLLG 240

>gi|17646388|gb|AAL40946.1|AF440787 1 (AF440787) interleukin 10 receptor 2 precu
 Length = 351

Score = 49.3 bits (116), Expect = 5e-05
 Identities = 57/247 (23%), Positives = 104/247 (42%), Gaps = 34/247 (13%)

Query: 27 LLTDEVAILPAPQNLSVLSTNMKHLWMSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
 LL + ++P P+ + + S N K++L W P + ++ +Y+ Y S + H
 Sbjct: 15 LLVPALGMIPPPEKVRMNSVNFKNILQWEVPAPKTNLTFTAQYE-SYRS-FQDH----- 67
 Query: 87 SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTS AW-SILKHPFNRNSTILTRPGMEI 145
 C T +CD + ++ Y +RVRA L + S W ++ P TI+ P M+I
 Sbjct: 68 --CKRTASTQCDFS-HLSKYGDYTVRVRAELADEHSEWVNVTFPCV--EDTIIGPPEMQI 122

Query: 146 KXXGFHLVIE-----LEDLGPQFEFLVAYWXREPGAEEHVKMVRSGGIPVH 191
 L + L+++ + + V YW + G E ++V V
 Sbjct: 123 ESLAESLHLRFSAPQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVS PYDSEV- 179

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQGEAIPVLALFAFVGFM LILVVVP 251
 L +EP YC++ Q F+ +S+ C + I V +LI+ V+
 Sbjct: 180 LRNLEPWTTCYCIQVQGFLLDQNRTGEWSEPICERTGNDEITPSW----IVAILIVSVLV 235

Query: 252 LFWVKMG 258
 +F++ +G
 Sbjct: 236 VFLFLLG 242

>gi|462415|sp|Q04790|INR1 BOVIN INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECURS
(IFN-ALPHA-REC)
gi|346520|pir|S27387 interferon alpha receptor type 1 precursor - bovine
gi|432|emb|CAA48484.1| (X68443) interferon receptor type 1 [Bos taurus]
Length = 560

Score = 49.3 bits (116), Expect = 6e-05

Identities = 65/299 (21%), Positives = 125/299 (41%), Gaps = 34/299 (11%)

Query: 21 YALIPCLLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEY-QGEYESLYT 79
Y+ + C+ T E +P+P+N+ + + N ++L W P E + ++ + ++ +
Sbjct: 215 YSPVYCINTTERHKVPSPENIQINADNQIYVLKWD---YPYENATFQAQWLRAFFKKIPG 271

Query: 80 SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHFPNRSNTI 137
+H W C C +++++ Y +RVRA+ G+ TS WS K TI
Sbjct: 272 NHSDKWKQIPNCENVSTHCVFPREVSSRGIYVVRASNGNGTSFWSEEKEFNTEMKTI 331

Query: 138 LTRPGMEIXK---XGFHLVI---ELEDLGPQ---FEFLVAYWXREPGAEEHVKMVRSG 186
+ P + + H+ + E E++ + V +W AE V R+
Sbjct: 332 IFPPVISVKSVTDDSLHVSVGASEESENMSVNLQYPLIYEVIFWENTSNAERKVLKRTN 391

Query: 187 GIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQ---GEAIPLVLALFAF 240
I ++P YCVKA+ ++ S+FS T C + + +V A
Sbjct: 392 FI---FPDLKPLTVYCVKARALIENDRRNKGSSFSQTVCEKTKPGNTSKTWLIVGTCTAL 448

Query: 241 VGFMILILVVVPLFVWKMGRLLQYSCCPVVVLPDITLK--ITNSPQK--LISCRREEVDAC 295
+++ VV +F+ R ++Y P P ++ ++ P + L+S E+ + C
Sbjct: 449 FSIPVVIYVSVFL---RCVKYVFFPSSKPPSSVDEYFSDQPLRNLLLSTSEEQTERC 503

>gi|6754302|ref|NP_034638.1| (NM_010508) interferon (alpha and beta) receptor; IN
[Mus musculus]
gi|462416|sp|P33896|INR1 MOUSE INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECURS
(IFN-ALPHA-REC)
gi|284965|pir|A45283 interferon alpha/beta receptor - mouse
gi|194112|gb|AAA37890.1| (M89641) interferon alpha/beta receptor [Mus musculus]
Length = 590

Score = 47.8 bits (112), Expect = 2e-04

Identities = 76/331 (22%), Positives = 138/331 (40%), Gaps = 29/331 (8%)

Query: 3 TFTMVLEEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGE 62
T+ + ++ I SL Y+ + C+ T +P P NL V + ++L W IA +
Sbjct: 197 TYCLEVKAIHPSLKKHSNYSTVQCISTTVANKMPVPGNLQVDAQGKSYVLKWD-YIASAD 255

Query: 63 TVYYSVEYQGEYESLYTSHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQ 120
++ + G +S SH W P C+ + C + D T + L V+A+ G+
Sbjct: 256 VLFRAQWLPYGYSKSSSGSHSDKWKPIPTCANVQTTHCVFSQDTVYTGTFFLHVQASEGNH 315

Query: 121 TSAWSILKHFPNRSNTILTRPGMEIXKXGFHLVIEL---EDLGPQFEFLVAYWXREPGE 177
TS WS K ++ + P + + L++ + + + +W E +
Sbjct: 316 TSFWSEEKFIDSQKHILPPPPVITVTAMSDTLVYVNCQDSTCDGLNYEIIIFW--ENTSN 373

Query: 178 EHVKMVRSGGIPVHLETMEPGAAYCVKAQTFVKA-IGXYSAFSQTECVXVQGEAIPLVLA 236
+ M + G L+ ++P YCV+A+ +A + S FS+ C + + +
Sbjct: 374 TKISMEKDGP-EFTLKNLQPLTVYCVQARVLFALLNKTSNFSEKLCEKTRPGSFSTIWI 432

Query: 237 LFAF-VGFMILILVVVPL-FVWKMGRLLQYSCCPVVVLPDITLK--ITNSPQK---LISCR 289
+ V F ++V+ L VWK L + C P + P ++ + P K L++
Sbjct: 433 ITGLGVVFFSVMVLYALRSVWKY---LCHVCFPPLKPPRSIDFFSEPPSKNLVLLTAE 489

Query: 290 -----EEVDACATAVM-SPEELLRAWIS 311
E D A V +PEE LR + S
Sbjct: 490 HTERCFIIENTDTVAVEVKHAPEEDLRKYSS 520

Score = 42.7 bits (99), Expect = 0.006

Identities = 38/201 (18%), Positives = 81/201 (39%), Gaps = 19/201 (9%)

Query: 35 LPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
 L P+N+ V + + L WS +V +S EY+ + E+ W+ C T
 Sbjct: 29 LKPPENIDVYIIDNYTLKWSSHGSMGSGVTFSAEYRTKDEAK-----WLKVPECQHTTT 83

Query: 95 PECDVT-DDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILTRPGMEIXKXGFHLV 153
 +C+ + D + RVRA G+ TS+W+ + + ++ P + + ++
 Sbjct: 84 TKCEFSLLDNTNVIKTQFRVRAEEGNSTSSWNEVDPFIPFYTAHMSPPFVRLEAEDKAIL 143

Query: 154 IELEDLG-----PQFEFLVAYWXREPAAEEHVKMVRSGGIPVHLETMEPGAAYCV 203
 + + G P F + + W + + K + S + + P YC+
 Sbjct: 144 VHISPPGQDGNMWALEKPSFSYTIQWQSSDK---KTINSTYYYVEKIPELLPETTYCL 200

Query: 204 KAQTFVKAIGXYSAFSQTCEV 224
 + + ++ +S +S +C+
 Sbjct: 201 EVKAIHPSLKKHSNYSTVQCI 221

>gi|20896187|ref|XP_128323.1| (XM_128323) similar to interleukin 10 receptor 2 pr
 musculus]
 Length = 351

Score = 47.4 bits (111), Expect = 2e-04

Identities = 56/247 (22%), Positives = 103/247 (41%), Gaps = 34/247 (13%)

Query: 27 LLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPS 86
 LL + ++P P+ + + S N K++L W P + ++ +Y+ Y S + H
 Sbjct: 15 LLVPALGMIPPEKVRMNSVNFKNILQWEVPAPFKNLTFTAQYE-SYRS-FQDH----- 67

Query: 87 SWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSASW-SILKHPFNRNSTILTRPGMEI 145
 C T +CD + ++ Y +RVRA L + S W ++ P TI+ P M+I
 Sbjct: 68 --CKRTASTQCDIFS-HLSKYGDYTVRVRRAELADEHSEWVNVTFPCV--EDTIIGPPEMQI 122

Query: 146 KXKXGFHLVIE-----LEDLGPQFEFLVAYWXREPAAEEHVKMVRSGGIPVH 191
 L + L+++ + + V YW + G E ++V V
 Sbjct: 123 ESLAESLHLRFSAEQIENEPETWTLKNIYDSWAYRVQYW--KNGTNEKFQVVSPLYDSEV- 179

Query: 192 LETMEPGAAYCVKAQTFVKAIGXYSAFSQTCEVXVQGEAIPVLALFAFVGFMILLVVP 251
 +EP YC++ Q F+ +S+ C + I V +LI+ V+
 Sbjct: 180 FGNLEPWTTCYCIQVQGFLLDQNRGTGEWSEPICERTGNDEITPSW----IVAILIVSVLV 235

Query: 252 LFWVKMG 258
 +F++ +G
 Sbjct: 236 VFLFLLG 242

>gi|163188|gb|AAA02571.1| (L06320) alpha-interferon receptor [Bos taurus]
 Length = 560

Score = 46.6 bits (109), Expect = 4e-04

Identities = 46/204 (22%), Positives = 87/204 (42%), Gaps = 20/204 (9%)

Query: 21 YALIPCLLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEY-QGEYESLYT 79
 Y+ + C+ T E +P+P+N+ + + N ++L W P E + ++ + ++ +
 Sbjct: 215 YSPVYCINTTERHKVPSPENIQINADNQIYVLKWD---YPYENATFQAQWLRAFFKKIPG 271

Query: 80 SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTI 137
 +H W C C +++++ Y +RVRA+ G+ TS WS K TI
 Sbjct: 272 NHSDKWKQIPNCENVSTSTHCVFPREVSSRGIIYVVRASNGNGTSFWSEEKEFNTEMKTI 331

Query: 138 LTRPGMEIXK---XGFHLVI----ELEDLGPQ----FEFLVAYWXREPAAEEHVKMVRSG 186
 + P + + H+ + E E++ + V +W AE V R+
 Sbjct: 332 IFPPVISVKSVTDDSLHVSVGASEESENMSVNQLYPLIYEVIFWENTSNAERKVLEKRTN 391

Query: 187 GIPVHLETMEPGAAYCVKAQTFVK 210

I ++P YCVKA+ ++

Sbjct: 392 FI---FPDLKPLTVYCVKARALIE 412

>gi|2612835|gb|AAB84231.1| (U65978) interferon alpha/beta receptor-1 [Ovis aries]
Length = 560

Score = 46.2 bits (108), Expect = 4e-04

Identities = 66/300 (22%), Positives = 113/300 (37%), Gaps = 36/300 (12%)

Query: 21 YALIPCLLTDEVAIIPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTS 80

Y+ + C+ T E +P+P+N+ + N ++L W + Y S +Q ++ +

Sbjct: 215 YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-----DYPYESTTFQAQWLRAFLK 267

Query: 81 HI-----WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHFPNR 133

I W C C DI + Y +RVRA+ G+ TS WS K FN

Sbjct: 268 KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWSEEKE-FNT 326

Query: 134 NSTILTRPGM----EIXKXGFHLVI----ELEDLGPQ----FEFLVAYWXREPAAEEHVK 181

+ P + I H+ + E E++ + V +W AE V

Sbjct: 327 EVKPIIFPPVISMKSITDDSLHVSVGASEESENMSVNQLYPLVYEVIFWENTSNAERKVL 386

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQGEAIPLVLALFA 239

R+ ++P YCVKA+ ++ S++S T C + +

Sbjct: 387 EKRTD---FTFPNLKPLTVYCVKARALIENDRWKNGSSYSDTVCEKTKPGNTSKTWLIAG 443

Query: 240 FVGFMILILVVVPLFVWKMGRLQLYSCCPVVVLPDTLKITNSPQK---LISCRREEVDAC 295

+ ++VV V R ++Y P P ++ S Q L+S E+ + C

Sbjct: 444 ICTALFSILVVIYVVRVFLRCVKYVFFPSSKPPSSVDQYFSDQPLRNLLLSTSEEQTERC 503

>gi|2494729|sp|Q28589|INR1 SHEEP INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECUR
(IFN-ALPHA-REC) (INTERFERON ALPHA/BETA RECEPTOR-1)

gi|1213627|emb|CAA65183.1| (X95939) type I interferon receptor [Ovis aries]
Length = 560

Score = 46.2 bits (108), Expect = 4e-04

Identities = 64/300 (21%), Positives = 110/300 (36%), Gaps = 36/300 (12%)

Query: 21 YALIPCLLTDEVAIIPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTS 80

Y+ + C+ T E +P+P+N+ + N ++L W + Y S +Q ++ +

Sbjct: 215 YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-----DYPYESTTFQAQWLRAFLK 267

Query: 81 HI-----WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHFPNR 133

I W C C DI + Y +RVRA+ G+ TS WS K FN

Sbjct: 268 KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWSEEKE-FNT 326

Query: 134 NSTILTRPGM----EIXKXGFHLVIELEDLGPQFE-----FLVAYWXREPAAEEHVK 181

+ P + I H+ + + + V +W AE V

Sbjct: 327 EVKPIIFPPVISMKSITDDSLHVSVSASEESENMSVNQLYPLVYEVIFWENTSNAERKVL 386

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQTFVK--AIGXYSAFSQTECVXVQGEAIPLVLALFA 239

R+ ++P YCVKA+ ++ S++S T C + +

Sbjct: 387 EKRTD---FTFPNLKPLTVYCVKARALIENDRWKNGSSYSDTVCEKTKPGNTSKTWLIAG 443

Query: 240 FVGFMILILVVVPLFVWKMGRLQLYSCCPVVVLPDTLKITNSPQK---LISCRREEVDAC 295

+ ++VV V R ++Y P P ++ S Q L+S E+ + C

Sbjct: 444 ICTALFSILVVIYVVRVFLRCVKYVFFPSSKPPSSVDQYFSDQPLRNLLLSTSEEQTERC 503

>gi|6680373|ref|NP_032364.1| (NM_008338) interferon gamma receptor 2 [Mus musculus]

gi|627892|pir|A49947 interferon gamma receptor beta subunit - mouse

gi|545842|gb|AAB30165.1| (S69336) interferon gamma receptor beta subunit; IFN-gamma
chain; IFN-gamma R species-specific cofactor [Mus sp.]

gi|1710144|gb|AAC52938.1| (U69599) ifngr2 [Mus musculus]

Length = 332

Score = 46.2 bits (108), Expect = 5e-04

Identities = 62/219 (28%), Positives = 91/219 (41%), Gaps = 38/219 (17%)

Query: 30 DEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWC 89
 D + L A P N + N + +L W P +P V Y Q EY +I SW
 Sbjct: 24 DSFSQLAAPLNPRHLHLYNDEQILTWEPP--SPSSNDPRPVVYQVEYS-----FIDGSWH 74

Query: 90 SLTEGPEC-DVTD---DITA-----TVPYN--LRVRATLGSQTSAWSILKHPFNRNST 136
 L E P C D+T+ D+T P+ LRVRA G+ TS W L+ PF
 Sbjct: 75 RLLE-PNCTDITETKCDLTGGGRLKLFHPFTVFLRVRAKRGNLTSKWVGLE-PFQHYEN 132

Query: 137 ILTRP--GMEIXKXGFHLVIELE---DL--GPQFEFLVAYWXREPAAEHVK-MVRSGGI 188
 + P + + LVI D+ G F++LV YW + +E V+ +S I
 Sbjct: 133 VTGPPKNISVTPGKGS�VIHFSPFPDVFHGATFQYLHYWEKSETQQEQVEGPFKSNSI 192

Query: 189 PVHLETMEPGAAYCVKAQTFV----KAIGXSAFSQTEC 223
 L ++P YC++ + + K I + S C
 Sbjct: 193 V--LGNLKPYPVYCLQTEAQLILKNKKIRPHGLLSNVSC 229

>gi|7657691|ref|NP_055247.1| (NM_014432) interleukin 20 receptor, alpha; class II
 receptor ZCYTOR7 [Homo sapiens]
 gi|6013325|gb|AAF01320.1|AF184971.1 (AF184971) class II cytokine receptor ZCYTOR
 Length = 553

Score = 45.8 bits (107), Expect = 6e-04

Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWC SLTE 93
 LP P N++ LS NMK++L W+P G V Y+V+Y +Y W+ S C
 Sbjct: 37 LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94 GPECVDTDITA-TVPYNLRVRATLGSQTSAWS 125
 CD++ + + Y +V+A G++ S W+
 Sbjct: 92 RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124

>gi|12732140|ref|XP_004438.2| (XM_004438) interleukin 20 receptor, alpha [Homo sa
 gi|14031069|emb|CAC38375.1| (AL135902) bA204P2.1.1 (interleukin 20 receptor alpha
 [Homo sapiens]
 Length = 553

Score = 45.8 bits (107), Expect = 6e-04

Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWC SLTE 93
 LP P N++ LS NMK++L W+P G V Y+V+Y +Y W+ S C
 Sbjct: 37 LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94 GPECVDTDITA-TVPYNLRVRATLGSQTSAWS 125
 CD++ + + Y +V+A G++ S W+
 Sbjct: 92 RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124

>gi|14031070|emb|CAC38376.1| (AL135902) bA204P2.1.3 (interleukin 20 receptor alpha
 [Homo sapiens]
 Length = 209

Score = 45.4 bits (106), Expect = 9e-04

Identities = 29/93 (31%), Positives = 47/93 (50%), Gaps = 7/93 (7%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWC SLTE 93
 LP P N++ LS NMK++L W+P G V Y+V+Y +Y W+ S C
 Sbjct: 37 LPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQY-----FIYGQKKWLNKSECRNIN 91

Query: 94 GPECVDTDIT-ATVPYNLRVRATLGSQTSAWS 125
 CD++ + + Y +V+A G++ S W+
 Sbjct: 92 RTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWA 124

>gi|6680389|ref|NP_032374.1| (NM_008348) interleukin 10 receptor, alpha [Mus musc
gi|20888213|ref|XP_125167.1| (XM_125167) interleukin 10 receptor, alpha [Mus mus
gi|3024007|sp|Q61727|I10R MOUSE Interleukin-10 receptor alpha chain precursor (IL
gi|2137457|pir|A49667 interleukin-10 receptor - mouse
gi|437616|gb|AAA16156.1| (L12120) interleukin-10 receptor [Mus musculus]
Length = 575

Score = 45.1 bits (105), Expect = 0.001

Identities = 31/109 (28%), Positives = 46/109 (41%), Gaps = 9/109 (8%)

Query: 35 LPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94

LP+P + + +H+L W P+ E+ YY V + Y + W C +

Sbjct: 26 LPSPSYVWFEARFFQHILHWKPIPNQSESTYYEVALKQ-----YGNSTWNDIHCRAQA 80

Query: 95 PECDVDT---DDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139

CD+T D + Y RVRA SQ S W+ + F + ILT

Sbjct: 81 LSCDLTTFTLDLYHRSYGYRARVRAVDNSQYSNWTTTTETRTVDEVILT 129

>gi|20856437|ref|XP_136952.1| (XM_136952) similar to ba204P2.1.1 (interleukin 20
isoform 1) [Mus musculus]
Length = 560

Score = 43.9 bits (102), Expect = 0.002

Identities = 51/222 (22%), Positives = 91/222 (40%), Gaps = 33/222 (14%)

Query: 23 LIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIA-PGETVYYSVEYQGEYESLYTSH 81

L+PC+ LP P N++ LS NMK++L W+P + G V Y+V+Y +Y

Sbjct: 46 LVPCVFCG----LPKPTNITFLSINMKNVLHWNPPESLHGVEVITYTVQY-----FIYGQK 96

Query: 82 IWIPSSWCSLTEGPECDVTDDIT-ATVPYNLRVRATLGSQTSAWSILK--HPFNRN---- 134

W+ +S C CD++ + + + +V+A ++ S W+ + +PF

Sbjct: 97 KWLNASKCGSINRTYCDLSVETSDYEHQFYAKVKAIWEARCSEWAETERFYPPLETQVSP 156

Query: 135 -----STILTRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVKM 182

S LT P H V ++ + P ++ V+ + + +

Sbjct: 157 PEVALTTGEKSISIALTAPEKWKRNPDQHTV-SMQQIYPNLKYNVSVYNTKSRRTWSQCV 215

Query: 183 VRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXYSAFSQTECV 224

S + L +EP YCV ++ V SQ +C+

Sbjct: 216 TNSTLV---LSWLEPNTLYCVHVESLVPGPRLPMPSPKQKCI 254

>gi|10835183|ref|NP_000620.1| (NM_000629) interferon (alpha, beta and omega) rece
interferon-alpha receptor (HuIFN-alpha-Rec) [Homo
sapiens]

gi|124462|sp|P17181|INR1 HUMAN Interferon-alpha/beta receptor alpha chain precurs
(IFN-alpha-REC)

gi|106790|pir|A32694 interferon alpha/beta receptor precursor - human

gi|306914|gb|AAA52730.1| (J03171) interferon-alpha receptor precursor [Homo sapi
Length = 557

Score = 43.1 bits (100), Expect = 0.005

Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21 YALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYT- 79

Y+ + C+ T LP P+N+ V N ++L W + Y ++ +Q ++ +

Sbjct: 215 YSPVHCICKTTVENELPPPENIEVSVQNQNYVLKW-----DYTYANMTFQVQWLHAFK 267

Query: 80 ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHPFN 133

+H+ W C + +C ++ Y LRV+A+ G+ TS WS

Sbjct: 268 RNPNGNHLKWKQIPDCENVKTTQCVPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE-----LEDLGPQFEFLVAYWXREPGAEEHV 181

L P I FH+ I ++D +E + +W AE +

Sbjct: 328 IQAFLLPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPVLALFA 239
 ++ V + ++P YCVKA+ T + + S FS C + ++

Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMILILVVVPLFVWKMGRLQLYSCCPVVVLPDTLKITNS-----PQK--LISCRR 289
 VG + L +P ++ L+ C V P +LK ++S P K L+S

Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLSTSE 496

Query: 290 EEVDAC 295
 E+++ C

Sbjct: 497 EQIEKC 502

>gi|16166194|ref|XP_048562.2| (XM_048562) similar to interferon (alpha, beta and
 1; human interferon-alpha receptor (HuIFN-alpha-Rec)
 [Homo sapiens]
 gi|18255502|gb|AAH21825.1|AAH21825 (BC021825) Unknown (protein for MGC:24928) [Ho
 Length = 557

Score = 42.7 bits (99), Expect = 0.005

Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21 YALIPCLLTDEVAAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYT- 79
 Y+ + C+ T LP P+N+ V N ++L W + Y ++ +Q ++ +

Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-----DYTYANMTFQVQWLHAFK 267

Query: 80 ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHFPNR 133
 +H+ W C + +C ++ Y LRV+A+ G+ TS WS

Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE-----LEDLGPQFEFLVAYWXREPGEAEHVK 181
 L P I FH+ I ++D +E + +W AE +

Sbjct: 328 IQAFLLPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385

Query: 182 MVRSGGIPVHLETMEPGAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPVLALFA 239
 ++ V + ++P YCVKA+ T + + S FS C + ++

Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMILILVVVPLFVWKMGRLQLYSCCPVVVLPDTLKITNS-----PQK--LISCRR 289
 VG + L +P ++ L+ C V P +LK ++S P K L+S

Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLSTSE 496

Query: 290 EEVDAC 295
 E+++ C

Sbjct: 497 EQIEKC 502

>gi|32672|emb|CAA42992.1| (X60459) interferon alpha/beta receptor [Homo sapiens]
 Length = 557

Score = 42.7 bits (99), Expect = 0.005

Identities = 67/306 (21%), Positives = 120/306 (38%), Gaps = 49/306 (16%)

Query: 21 YALIPCLLTDEVAAILPAPQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYT- 79
 Y+ + C+ T LP P+N+ V N ++L W + Y ++ +Q ++ +

Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSVQNQNYVLKW-----DYTYANMTFQVQWLHAFK 267

Query: 80 ----SHI--WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSILKHFPNR 133
 +H+ W C + +C ++ Y LRV+A+ G+ TS WS

Sbjct: 268 RNPGNHLYKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSEEIKFDTE 327

Query: 134 NSTILTRPGMEI--XKXGFHLVIE-----LEDLGPQFEFLVAYWXREPGEAEHVK 181
 L P I FH+ I ++D +E + +W AE +

Sbjct: 328 IQAFLLPVFNIRSLSDSFHIYIGAPKQSGNTPVIQDYPLIYEII--FWENTSNAERKII 385

Query: 182 MVRSGGIPVHLETMPEGAAAYCVKAQ--TFVKAIGXYSAFSQTECVXVQGEAIPVLALFA 239
 ++ V + ++P YCVKA+ T + + S FS C + ++
 Sbjct: 386 EKKTD---VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWL 439

Query: 240 FVGFMILILVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS-----PQK--LISCRR 289
 VG + L +P ++ L+ C V P +LK ++S P K L+S
 Sbjct: 440 IVGICIALFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLSTSE 496

Query: 290 EEVDAC 295
 E+++ C
 Sbjct: 497 EQIEKC 502

>gi|4028137|gb|AAD13670.1| (AF082665) interferon alpha/beta receptor 2 [Gallus gal
 Length = 508

Score = 42.0 bits (97), Expect = 0.009
 Identities = 65/265 (24%), Positives = 106/265 (39%), Gaps = 43/265 (16%)

Query: 38 PQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTEGPE 96
 P NL + S N +H+L W P YY V LY+SH W + CS P
 Sbjct: 37 PDNLQMTSNNFQHILSWRAHSDPTVPTYRV-----LYSSHSNWKIAKQCSRIVQPF 88

Query: 97 CDVTDDI-TATVPYNLRVRATLGSQTSAWSILKHP-----FNRNSTI-----L 138
 C++TDD + Y+ V++ +G++ S+L FN +S + +
 Sbjct: 89 CNLTDDFQVVSDEYSAFVQSFVGTEVFNSSLLHFSPLSETFLGPPEFNLSSCVHCINITI 148

Query: 139 TRPGMEIXKXGFHLVIELEDLGPQFEFLVAYWXREPGAEEHVK--MVRSGGIPVHLETM 195
 P + K G ++ L D+ + + + R G EEH + V + +E +
 Sbjct: 149 KLPPTHLRKNG--KLKSLFDIYNKVNYEIT--LRTVG-EEHKRSPEKVTEEPFSIVIEEL 203

Query: 196 EPGAAYCVKAQTFVKAIGXYSAFSQTECVXVQ--GEAIPVLALFAFVGFMILILVVVPLF 253
 P YCV ++ +S S +C+ E + + + F +ILVV+
 Sbjct: 204 YPNRNYCVSVMV-TASLNKHSIPSAWKICITDSVAEKDYYGITIAGAICFSIILVILKC 262

Query: 254 VWKMGRLQLQYSCCPVVVLPDTLKIT 278
 + G +L LPDTL T
 Sbjct: 263 LHLGGYILHKKS----LPDTLVFT 282

>gi|4028141|gb|AAD13677.1| (AF082667) interferon alpha/beta receptor 2 [Gallus gal
 Length = 508

Score = 41.6 bits (96), Expect = 0.010
 Identities = 29/92 (31%), Positives = 44/92 (47%), Gaps = 10/92 (10%)

Query: 38 PQNLSVLSTNMKHLMLWSPVIAPGETVYYSVEYQGEYESLYTSHI-WIPSSWCSLTEGPE 96
 P NL + S N +H+L W P YY V LY+SH W + CS P
 Sbjct: 37 PDNLQMTSNNFQHILSWRAHSDPTVPTYRV-----LYSSHSNWKIAKQCSRIVQPF 88

Query: 97 CDVTDDI-TATVPYNLRVRATLGSQTSAWSIL 127
 C++TDD + Y+ V++ +G++ S+L
 Sbjct: 89 CNLTDDFQVVSDEYSAFVQSFVGTEVFNSSLL 120

>gi|16418459|ref|NP_443194.1| (NM_052962) class II cytokine receptor; interleukin
 protein [Homo sapiens]
gi|15212828|gb|AAK85715.1| (AY040567) interleukin 22-binding protein CRF2-10L [H
gi|16304593|emb|CAC85635.1| (AJ313162) soluble cytokine class II receptor, long i
 sapiens]
 Length = 263

Score = 41.6 bits (96), Expect = 0.011
 Identities = 51/232 (21%), Positives = 83/232 (34%), Gaps = 43/232 (18%)

Query: 38 PQNLSVLSTNMKHLMLWSPVIA-PGETVYYSVEYQGEYE-SLYTSHIWIPSSW----- 88
 PQ + S N ++L W P A G + Y V+Y+ + S+ +SH W
 Sbjct: 31 PQRVQFQSRNFHNLQWQGRALTGNSSVYFVQYKIMFSCSMKSSHQKPSGCWQHISCNF 90

Query: 89 -----CSLTEGPECDVTDIT-ATVPYNLRVRATLGSQTSAWSILK 128
 C T+ CD+T + + PY RVRA S WS+
 Sbjct: 91 PGCRTLAKYGQRQWKNECDWGTQELSCDLTSETSDIQEPYGRVRAASAGSYSEWSMTP 150

Query: 129 HPFNRNSTILTRPGMEIXKXGFHLVIELE-----DLGPQFEFLVAYWXREP 174
 T + P M I + L++ L + +E L +
 Sbjct: 151 RFTPWWETKIDPPVMNITQVNGSLLVILHAPNLPYRYQKEKNVSIEDYYELLYRVFIINN 210

Query: 175 GAEHVVMVRSGGIPVHLETMEPGAAYCVKAQTFVKAIGXSAFSQTECVXV 226
 E+ K+ V +E + P ++YCV A+ + + S S+ CV +
 Sbjct: 211 SLEKEQKVYEGAHRAVEIEALTPHSSYCVVAEIQPMLDRRSQRSEERCVEI 262

>gi|15988304|pdb|1J7V|R Chain R, Human IL-10 IL-10r1 Complex
 Length = 214

Score = 40.8 bits (94), Expect = 0.019
 Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

Query: 35 LPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
 LP+P ++ + H+L W+P+ E+ Y V Y W S CS T
 Sbjct: 5 LPSPPSVWFEEFFHHILHWTPIQQSESTCYEVAL-----RYGIESWNSISQCSQTLS 59

Query: 95 PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
 + VT D+ + Y RVRA GS+ S W++ F+ + LT
 Sbjct: 60 YDLTAVTLDLYHSNGYRARVRAVDGSRHSQWTVTNTFRFSVDEVTLT 105

>gi|106794|pir||S17112 interferon alpha/beta receptor - human
 Length = 545

Score = 40.8 bits (94), Expect = 0.021
 Identities = 66/299 (22%), Positives = 120/299 (40%), Gaps = 47/299 (15%)

Query: 21 YALIPCLLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYT- 79
 Y+ + C+ T LP P+N+ V N ++L W + Y ++ +Q ++ +
 Sbjct: 215 YSPVHCIKTTVENELPPPENIEVSQVQNYVLKW-----DYTYANMTFQVQWLHAFK 267

Query: 80 ----SHI--WIPSSWCSLTEGPECDVTDITATVPYNLRVRATLGSQTSAWSILKHPFNR 133
 +H+ W C + +C ++ Y LRV+A+ G+ TS WS
 Sbjct: 268 RNPNGNHLKWKQIPDCENVKTTQCVFPQNVFQKGIYLLRVQASDGNNTSFWSS---EEIKF 324

Query: 134 NSTILTRPGMEI-----XKXGFHLVIELEDLGPQFEFLVAYWXREPGEHVVMVRSGGI 188
 ++ I I + G VI +D +E + +W AE + ++
 Sbjct: 325 DTEIQVSDSFHIYIGAPKQSGNTPVI--QDYPLIYEII--FWENTSNAERKIEKKT-- 378

Query: 189 PVHLETMEPGAAYCVKAQ--TFVKAIGXSAFSQTECVXVQGEAIPVLALFAVGFMLI 246
 V + ++P YCVKA+ T + + S FS C + ++ VG +
 Sbjct: 379 -VTVPNLKPLTVYCVKARAHTMDEKLNKSSVFSDAVCEKTKPGNTS---KIWLIVIGICIA 434

Query: 247 LVVVPLFVWKMGRLLQYSCCPVVVLPDTLKITNS-----PQK--LISCRREEVDAC 295
 L +P ++ L+ C V P +LK ++S P K L+S E+++ C
 Sbjct: 435 LFALPFVIYAAKVFLR--CINYVFFP-SLKPSSSIDEYFSEQPLKNLLLSTSEEQIEKC 490

>gi|4504633|ref|NP_001549.1| (NM_001558) interleukin 10 receptor, alpha; Interleu
 [Homo sapiens]
 gi|3024000|sp|Q13651|I10R HUMAN Interleukin-10 receptor alpha chain precursor (IL
 gi|2135511|pir||I56215 interleukin-10 receptor - human
 gi|482803|gb|AAA17896.1| (U00672) interleukin-10 receptor [Homo sapiens]
 gi|20380860|gb|AAH28082.1| (BC028082) interleukin 10 receptor, alpha [Homo sapie
 Length = 578

Score = 40.0 bits (92), Expect = 0.036
 Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

Query: 35 LPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94

Sbjct: 26 LP+P ++ + H+L W+P+ E+ Y V Y W S CS T
 LPSPPSVWFEEFFHHILHWTPIPNQSESTCYEVALL-----RYGIESWNSISNCSQTLS 80

Query: 95 PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
 + VT D+ + Y RVRA GS+ S W++ F+ + LT

Sbjct: 81 YDLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLT 126

>gi|20560751|ref|XP_006447.7| (XM_006447) similar to Interleukin-10 receptor alph
 precursor (IL-10R-A) (IL-10R1) [Homo sapiens]
 Length = 578

Score = 40.0 bits (92), Expect = 0.036

Identities = 31/106 (29%), Positives = 47/106 (44%), Gaps = 6/106 (5%)

Query: 35 LPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
 LP+P ++ + H+L W+P+ E+ Y V Y W S CS T

Sbjct: 26 LPSPPSVWFEEFFHHILHWTPIPNQSESTCYEVALL-----RYGIESWNSISNCSQTLS 80

Query: 95 PECD-VTDDITATVPYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
 + VT D+ + Y RVRA GS+ S W++ F+ + LT

Sbjct: 81 YDLTAVTLDLYHSNGYRARVRAVDGSRHSNWTVTNTRFSVDEVTLT 126

>gi|11991877|gb|AAG42376.1|AF296666_1 (AF296666) type I interferon receptor 1e [Ov
 Length = 332

Score = 39.7 bits (91), Expect = 0.044

Identities = 29/112 (25%), Positives = 48/112 (41%), Gaps = 14/112 (12%)

Query: 21 YALIPCLLTDEVAILPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYESLYTS 80
 Y+ + C+ T E +P+P+N+ + N ++L W + Y S +Q ++ +

Sbjct: 215 YSPVYCINTTERHKVPSPENVQINVDNQAYVLKW-----DYPYESTTFQAQWLRAFLK 267

Query: 81 HI-----WIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWS 125
 I W C C DI + Y +RVRA+ G+ TS WS

Sbjct: 268 KIPGKHSNKWKQIPNCENVTTTHCVFPRDIFSMGIYYVRVRASNGNGTSFWS 319

>gi|15212830|gb|AAK85716.1| (AY040568) interleukin 22-binding protein CRF2-10S [H
 Length = 130

Score = 38.5 bits (88), Expect = 0.087

Identities = 28/91 (30%), Positives = 40/91 (43%), Gaps = 7/91 (7%)

Query: 38 PQNLSVLSTNMKLLMWSPVIA-PGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPE 96
 PQ + S N ++L W P A G + Y V+Y+ +Y W C T+

Sbjct: 31 PQRVQFQSRNFHNLQWQGRALTGNSSVYFVQYK-----IYGQRQWKNKEDCWGTQELS 85

Query: 97 CDVTDDIT-ATVPYNLRVRATLGSQTSAWSI 126
 CD+T + + PY RVRA S WS+

Sbjct: 86 CDLTSETSDIQEPYYGRVRAASAGSYSEWSM 116

>gi|20896935|ref|XP_139651.1| (XM_139651) similar to INTERFERON-ALPHA/BETA RECEPT
 PRECURSOR (IFN-ALPHA-REC) [Mus musculus]
 Length = 179

Score = 35.4 bits (80), Expect = 0.80

Identities = 24/94 (25%), Positives = 42/94 (44%), Gaps = 11/94 (11%)

Query: 35 LPAPQNLSVLSTNMKLLMWSPVIAPGETVYYSVEYQGEYES---LYTSHIWIPSSWCSL 91
 L P+N T+ + L WS + + + G+++S + + W P C+

Sbjct: 61 LEPPENGDACVTDNRFTLKWSS-----HGLLPFSGQWDSFNRISSRDKWKPIPTCAD 112

Query: 92 TEGPECDVTDDITATVPYNLRVRATLGSQTSAWS 125
 + C + D T + LRV+A+ G+ TS WS

Sbjct: 113 VQTTHCVFSQDVTYTGTFLLRVQASEGNHTSFWS 146

>gi|18547428|ref|XP_089078.1| (XM_089078) similar to interleukin-22 binding prote
sapiens]
 Length = 423

Score = 35.4 bits (80), Expect = 0.85

Identities = 54/208 (25%), Positives = 89/208 (41%), Gaps = 25/208 (12%)

Query: 35 LPAPQNL SVLSTNMKHL LMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEG 94
 L PQN+++LS N L W P + + V Y V YQ S T W C+ T+
 Sbjct: 24 LAPPQNVTL LLSQNF SVYLTWLPGLGNPQDVITYFVAYQ----SSPTRRRWREVEECAGTKE 79

Query: 95 PECDV----TDDITATVPYNLRVRATLGSQTSAW---SILKHPFNRNST----ILTRPGM 143
 C + D+ + RVR S S W L + F +LT+
 Sbjct: 80 LLCMMCLKKQDLYNK--FKGRVRTVSPSSKSPWVESEYLDYLFVEVPAPPVLVLQTTEE 137

Query: 144 EIXKXG-FHLVIELEDLGPQFEFLVAYWXREP GAEHVKMVRSGGIPVHLETMEPGAA-- 200
 + + L + L ++E VA+W +E + + V G PV + T++P A+
 Sbjct: 138 ILSANATYQLPPCMPPLDLKYE--VAFW-KEGAGNKTLFPVTPHGPVQI-TLQPAASEH 193

Query: 201 YCVKAQT-FVKAIGXYSAFSQTECVXVQ 227
 +C+ A+T + ++ YS FS+ C ++
 Sbjct: 194 HCLSARTIYTFSVPKYSKFSKPTCFLLE 221

>gi|15602147|ref|NP_245219.1| (NC_002663) unknown [Pasteurella multocida]
gi|12720514|gb|AAK02366.1| (AE006063) unknown [Pasteurella multocida]
 Length = 517

Score = 33.5 bits (75), Expect = 3.6

Identities = 21/63 (33%), Positives = 34/63 (53%), Gaps = 3/63 (4%)

Query: 118 GSQTSAWSILKHPFNRNSTILTRP--GMEIXKXGFH-LVIELEDLGPQFEFLVAYWXREP 174
 G +T A+ ++ F N ILTR G+E+ K GFH L+ E + G +E ++ + +
 Sbjct: 430 GIETKAYRLVTETFGENIGILTREVFGEVEKSGFHKLLNESVNKGGTYESILESINYQL 489

Query: 175 GAE 177
 G E
 Sbjct: 490 GKE 492

>gi|2129405|pir|S53867 DNA (cytosine)-methyltransferase (EC 2.1.1.-) Dcm5a - Halo
salinarum
gi|732794|emb|CAA56444.1| (X80164) cytosine methylase [Bacteriophage phi-H]
 Length = 245

Score = 33.1 bits (74), Expect = 4.6

Identities = 23/75 (30%), Positives = 32/75 (42%), Gaps = 7/75 (9%)

Query: 54 WSPVIAPGETVY-Y SVEYQGEYESLYTSHIWIPSSWCSLTEGPEC DVTDDITATVPYNLR 112
 W P I E + ++ Y E LY ++ P S LT GPEC + P + +
 Sbjct: 45 WKPAIRTHEENHG WANHYHARIEELYPPNVVDPGSVTLLTGPECTHFSNARGGKPVSDQ 104

Query: 113 VRATLGSQTSAWSIL 127
 RA SAW +L
 Sbjct: 105 KRA-----SAWHVL 113

>gi|3980170|emb|CAA37597.1| (X53521) brain tissue factor [Oryctolagus cuniculus]
 Length = 260

Score = 32.3 bits (72), Expect = 6.8

Identities = 31/102 (30%), Positives = 42/102 (40%), Gaps = 13/102 (12%)

Query: 40 NLSVLSTNMKHL LMWSPVIAPGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPEC DVT 99
 NL+ STN K +L W P Y+V+ E+ W S C LT ECD+
 Sbjct: 9 NLTWKSTNFKTILEWEP---KSIDHVYTVQISTRLEN-----W--KSKCFLTAETECDL 57

Query: 100 TDDITATV--PYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139

TD++ V Y RV + + + P RNS T
 Sbjct: 58 TDEVVKDVGQTYMARVLSYPARNGNTTGFPEEPPFRNSPEFT 99

>gi|3212253|pdb|1A21|B Chain B, Tissue Factor (Tf) From Rabbit
 gi|3212252|pdb|1A21|A Chain A, Tissue Factor (Tf) From Rabbit
 Length = 219

Score = 32.3 bits (72), Expect = 7.0

Identities = 31/102 (30%), Positives = 42/102 (40%), Gaps = 13/102 (12%)

Query: 40 NLSVLSTNMKHLMLWSPVIAPIGETVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDV 99
 NL+ STN K +L W P Y+V+ E+ W S C LT ECD+
 Sbjct: 9 NLTWKSTNFKTILEWEP---KSIDHVYTVQISTRLEN-----W--KSKCFLTAETECDL 57

Query: 100 TDDITATV--PYNLRVRATLGSQTSAWSILKHPFNRNSTILT 139
 TD++ V Y RV + + + P RNS T
 Sbjct: 58 TDEVVKDVGQTYMARVLSYPARNGNTTGFPEEPPFRNSPEFT 99

Database: All non-redundant GenBank CDS
 translations+PDB+SwissProt+PIR+PRF
 Posted date: Aug 8, 2002 12:48 AM
 Number of letters in database: 330,262,426
 Number of sequences in database: 1,047,264

Lambda K H
 0.323 0.137 0.434

Gapped
 Lambda K H
 0.267 0.0410 0.140

Matrix: BLOSUM62

Gap Penalties: Existence: 11, Extension: 1

Number of Hits to DB: 206,395,047

Number of Sequences: 1047264

Number of extensions: 8248875

Number of successful extensions: 17962

Number of sequences better than 10.0: 58

Number of HSP's better than 10.0 without gapping: 14

Number of HSP's successfully gapped in prelim test: 44

Number of HSP's that attempted gapping in prelim test: 17876

Number of HSP's gapped (non-prelim): 73

length of query: 311

length of database: 330,262,426

effective HSP length: 121

effective length of query: 190

effective length of database: 203,543,482

effective search space: 38673261580

effective search space used: 38673261580

T: 11

A: 40

X1: 16 (7.5 bits)

X2: 38 (14.6 bits)

X3: 64 (24.7 bits)

S1: 41 (22.0 bits)

S2: 71 (32.0 bits)

Cutting Edge: STAT Activation By IL-19, IL-20 and mda-7 Through IL-20 Receptor Complexes of Two Types¹

Laure Dumoutier,* Caroline Leemans,* Diane Lejeune,*
Sergei V. Kotenko,[†] and Jean-Christophe Renauld^{2*}

IL-10-related cytokines include IL-20 and IL-22, which induce, respectively, keratinocyte proliferation and acute phase production by hepatocytes, as well as IL-19, melanoma differentiation-associated gene 7, and AK155, three cytokines for which no activity nor receptor complex has been described thus far. Here, we show that mda-7 and IL-19 bind to the previously described IL-20R complex, composed by cytokine receptor family 2-8/IL-20R α and DIRS1/IL-20R β (type I IL-20R). In addition, mda-7 and IL-20, but not IL-19, bind to another receptor complex, composed by IL-22R and DIRS1/IL-20R β (type II IL-20R). In both cases, binding of the ligands results in STAT3 phosphorylation and activation of a minimal promoter including STAT-binding sites. Taken together, these results demonstrate that: 1) IL-20 induces STAT activation through IL-20R complexes of two types; 2) mda-7 and IL-20 redundantly signal through both complexes; and 3) IL-19 signals only through the type I IL-20R complex. *The Journal of Immunology*, 2001, 167: 3545–3549.

Recently, a family of other cytokines with limited homology to IL-10 have been described (1). The first IL-10 homolog was called melanoma differentiation-associated gene 7 (mda-7)³ because its expression was up-regulated during the in vitro differentiation of a melanoma cell line (2). Although this protein shows 22% amino acid identity with IL-10, it was not originally recognized as a secreted protein, and its biological activities remain poorly understood. The mouse ortholog of mda-7 was identified recently as a Th2-specific cytokine and called FISP,

for IL-4-induced secreted protein (3). Its rat counterpart, called mob5, was suggested to play a role in ras oncogene-mediated neoplasia (4).

The *IL10* and *MDA7* genes have been mapped on chromosome 1q31–32, in a region where two additional IL-10-related genes, *IL19* and *IL20*, also were located. Little is known about IL-19, except that this gene is expressed by LPS-activated monocytes (5). The biological activities of IL-20 have been studied by using transgenic mice overexpressing this cytokine. These mice are characterized by neonatal lethality with skin abnormalities, including aberrant epidermal differentiation reminiscent of psoriasis lesions in human (6). An IL-20R complex was described as a heterodimer of two orphan class II cytokine receptor subunits: corticotropin-releasing factor (CRF) 2–8, proposed to be renamed IL-20R α , and DIRS1, designated IL-20R β (6).

In addition to the chromosome 1q31–32 cluster, two other IL-10-related cytokines, AK155 and IL-22, are located on human chromosome 12q15, near the IFN- γ gene. AK155 is known to be up-regulated by *Herpes saimiri* infection of T lymphocytes, but its activity and receptor remain unknown (7). IL-22 was described originally as an IL-9-inducible gene and called IL-TIF, for IL-10-related T cell-derived inducible factor (8). IL-22 activities include induction of the acute phase response in hepatocytes and are mediated through a heterodimeric receptor composed of the CRF2–9/IL-22R subunit and the β -chain of IL-10R (9–11). In addition to its cellular receptor, IL-22 binds to a secreted member of the class II cytokine receptor family, which was called IL-22BP, and appears to act as a natural IL-22 antagonist (12, 13).

Materials and Methods

Cell cultures and cytokines

HT-29 intestinal epithelial cells were grown in IMDM medium supplemented with 10% FCS, 0.55 mM L-arginine, 0.24 mM L-asparagine, and 1.25 mM L-glutamine. Human embryonic kidney (HEK) 293-EBV nuclear Ag cells were grown in DMEM medium supplemented with 10% FCS. IL-10 homologs were produced by transient expression in HEK293-EBNA cells by the Lipofectamine 2000 method (Life Technologies, Gent, Belgium). The coding sequences for mda-7, IL-19, and IL-22 were amplified by RT-PCR from RNA of T cells stimulated with anti CD3 Ab. The IL-20 coding sequence was amplified from skin RNA. These cDNAs were cloned into pCEP4 plasmid (Invitrogen, Groningen, the Netherlands) under the control of the CMV promoter. mda-7-Flag, IL-19-flag, IL-20-flag and IL-22-flag were generated from the pCEP4-cytokine constructs by mutating the STOP codon and introducing a sequence encoding a C-terminal flag: Gly-Gly-Gly-Asp-Tyr-Lys-Asp-Asp-Asp-Asp-Lys. The IL-22BP-Ig fusion cDNA was produced as described before (12). For Western blot analysis, 10 μ l of HEK293 supernatant was mixed with Laemmli sample buffer and boiled for 5 min before SDS-PAGE and transfer onto a polyvinylidene difluoride membrane (Amersham, Arlington Heights, IL). The membrane

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³ Abbreviations used in this paper: mda-7, melanoma differentiation-associated gene 7; CRF, cytokine receptor family; HEK, human embryonic kidney.

was probed with biotinylated anti-flag Ab (25 μ g/ml) and with streptavidin-HRP (1/5000; Amersham). An ECL detection kit (Amersham) was used for expression of chemiluminescence. The chemiluminescence signal was detected and quantified with a Kodak (Rochester, NY) Digital Science Image Station 440CF. Anti-phospho-STAT3 Western blots were performed as described previously (8).

The DIRS1/IL-20R β cDNA was amplified by RT-PCR from K562 leukemia cells and cloned into pCEP4 plasmid. The IL-22R cDNA was amplified by RT-PCR from the HepG2 hepatoma cell line before cloning into the pEF-BOSpuro expression vector (14). The CRF2-8/IL-20R α cDNA was amplified by PCR from a human placenta cDNA library (Clontech Laboratories, Palo Alto, CA), and cloned into the pCDEF3 plasmid. Anti-IL-10R β and anti-flag Abs were purchased from Peprotech (London, U.K.) and from Sigma (Bornem, Belgium), respectively. To produce anti-hIL-22R Abs, we transfected P815 mastocytoma cells with the hIL-22R cDNA in the pEF-BOS plasmid before injection into DBA/2 mice. After rejection of the tumors, the sera of these mice had high titers of neutralizing anti-hIL-22R Abs and were used at a 1/500 dilution.

Luciferase assays

The cytokine response was assessed by measuring luciferase production by cells transfected with the pGRR5 construct, (provided by Dr P. Brennan, Imperial Cancer Research Fund, London, U.K.). This construct contains five copies of the STAT-binding site of the Fc γ R1 gene inserted upstream from a luciferase gene controlled by the TK promoter. Transfections of HT-29 and HEK293 cells were performed as follows.

HT-29 cells were electroporated (10^7 cells in 400 μ l, 250 V, 192 Ω , 1200 μ F) with 15 μ g of pGRR5 and 15 μ g of each receptor cDNA, separately or in combination. Transfected cells were seeded in 96-well plates, incubated for 5 h at 37°C, and then preincubated, or not, for 1 h with anti-IL-22R antiserum (1/500) or with anti-IL-10R β Abs (6 μ g/ml). Next, the cells were stimulated with each cytokine for 2 h. Luciferase activity was measured with the Lucite plus Assay System kit (Canberra-Packard, Meriden, CT) with a Top Count microplate scintillation counter (Canberra-Packard).

HEK293-EBNA cells were seeded in 24-well plates (Nunc, Roskilde, Denmark) for 24 h. Transfections were conducted by using the Lipofectamine method (Life Technologies, Gent, Belgium), with 500 ng of plasmid encoding IL-22R, IL-20R β , or IL-20R α and with 100 ng of pGRR5. As an internal control, we used 100 ng of pRL-TK vector (Promega, Madison, WI) containing the *Renilla* luciferase gene under the control of the TK promoter. After 20 h, transfected cells were stimulated with cytokines, and 2 h later, cells were pelleted and lysed. Luciferase activity was monitored with the Dual-Luciferase Reporter Assay System kit (Promega).

IL-22BP interaction assays

Specific interactions between IL-22BP and cytokine-flag fusion proteins were assessed directly or indirectly by ELISA, as follows. Reacti-Bind Maleic Anhydride Activated Polystyrene plates (Pierce, Rockford, IL)

were coated overnight at 4°C with 12.5 μ g/ml of anti-flag Ab in PBS. The plates were incubated 2 h at 37°C with 50 μ l of cytokine-flag fusion proteins (HEK293 supernatants). A total of 10% of supernatant of IL-22BP-Ig was added for 2 h, and bound IL-22BP-Ig was detected by using anti-mouse IgG3 polyclonal Abs coupled to peroxidase (Southern Biotechnology Associates, Birmingham, AL). The enzymatic activity was measured as described previously (12). In the indirect assay, we tested the inhibitory effect of IL-10 homologs on the binding of IL-22BP to IL-22. For this purpose, IL-22BP-Ig (10%) was preincubated with IL-10 homologs 2 h before incubation with Reacti-Bind plates (Pierce) that had been coated with rIL-22 as described previously (12).

Results

STAT activation by IL-10 homologs in class II cytokine receptor-transfected cells

To characterize the interactions between IL-10 homologs and receptors belonging to the class II cytokine receptor family, we expressed mda-7, IL-19, IL-20, and IL-22 as fusion proteins with a C-terminal flag sequence by transient transfection of HEK293 cells. Protein production was checked by Western blot with an Ab specific for the flag peptide (Fig. 1A). HEK293 cells secreted mda-7, IL-19, and IL-22 proteins with a heterogeneous MW of 23–30 kDa, most likely resulting from glycosylation. The IL-20-flag protein is secreted as a single band with a size of ~18 kDa, suggesting that this cytokine is not glycosylated. Quantification of the chemiluminescence signal indicated that IL-19 and IL-22 were produced at a similar level, whereas IL-20 and mda-7 were produced 7-fold less.

These HEK293 supernatants were used to assess the interaction with class II cytokine receptors. A first set of experiments were performed in HT-29 cells, which endogenously express IL-22R and IL-10R β . STAT activation induced by IL-22 was monitored with the pGRR5 luciferase reporter (9). As shown in Fig. 1B (*top left*), these cells failed to respond to the other IL-10 homologs. When HT-29 cells were transfected with the IL-20R β cDNA, both mda-7 and IL-20 induced luciferase production. Interestingly, this effect was completely blocked by an anti-IL-22R antiserum, suggesting that mda-7 and IL-20 can activate STAT factors through a new IL-20R complex composed by IL-22R and IL-20R β (Fig. 1B, *bottom left*).

When cells were transfected with both IL-20R α and IL-20R β cDNAs, they became responsive to mda-7, IL-20, and IL-19, and the luciferase production was not affected anymore by anti-IL-22R

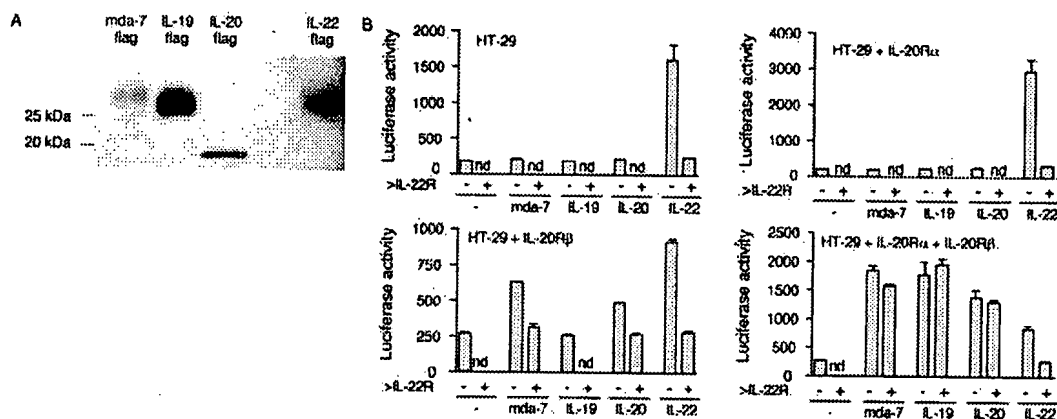


FIGURE 1. Human IL-10 homolog production and activity. *A*, The cDNAs encoding mda-7, IL-19, IL-20, and IL-22 tagged with a flag sequence were transfected in HEK293 cells. After 4 days, supernatants were analyzed by Western blotting with an Ab raised against the flag peptide. *B*, HT-29 cells were transfected with the pGRR5 luciferase construct with or without IL-20R α and IL-20R β as indicated. Cells were preincubated 1 h with or without anti-IL-22R antiserum (1/500) before stimulation with 1% of HEK293 supernatants. Luciferase activity was monitored 2 h later and is expressed in arbitrary units.

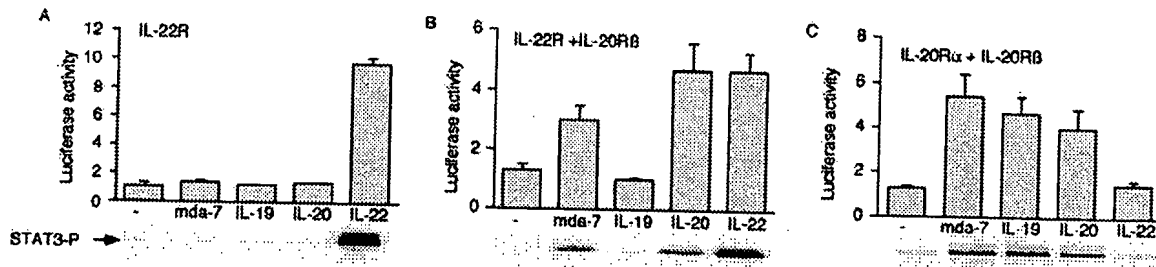


FIGURE 2. Activity of IL-10 homologs in HEK293 cells. HEK293 cells were transfected with the pGRR5 luciferase construct and cDNAs encoding IL-22R (A), IL-22R and IL-20R β (B), or IL-20R α and IL-20R β (C). Cells were stimulated with 10% of mda-7, IL-19, IL-20, or IL-22 supernatant. Luciferase activity was monitored 2 h later. The results are normalized by using *Renilla* luciferase as an internal control. Western blot analysis for STAT3 phosphorylation was performed after 15 min of stimulation.

Abs (Fig. 1B, bottom right), indicating that this activity was independent from this chain. Finally, on transfection with the IL-20R α cDNA alone, we failed to detect any response to mda-7, IL-19, and IL-20 (Fig. 1B, top right), confirming that IL-20R β is required for this process.

To characterize further the different types of receptor complexes, we used HEK293 cells, which express endogenous IL-10R β but not IL-22R. Untransfected HEK293 cells did not respond to any IL-10 homolog (data not shown). When the IL-22R cDNA was transfected, only IL-22 induced luciferase production and STAT-3 phosphorylation (Fig. 2A). Cells transfected with IL-22R and IL-20R β responded not only to IL-22 but also to IL-20 and mda-7 (Fig. 2B), whereas IL-20R β alone did not confer any cytokine responsiveness (data not shown). Transfection of both IL-20R α and IL-20R β cDNAs allowed for STAT activation by mda-7, IL-19, and IL-20, but not IL-22 (Fig. 2C). No response was observed in cells transfected with the IL-20R α cDNA alone (data not shown). In all cases, luciferase induction correlated with phosphorylation of STAT-3, as analyzed by Western blotting (Fig. 2). Similar results were obtained with HEK293 supernatants containing the wild-type cytokines.

Comparison of IL-20 and mda-7 sensitivity conferred by both types of IL-20R complexes

The observation that two different receptor complexes allowed for the response to IL-20 and mda-7 raised the possibility that each complex would respond preferentially to one cytokine. To test this hypothesis, we analyzed the response of HT-29 cells, transfected either with IL-20R β alone or both IL-20R α and IL-20R β , to different dilutions of mda-7, IL-19, and IL-20 supernatants. When both IL-20R α and IL-20R β were transfected, mda-7 and IL-20 dilutions showed a similar dose-response curve, indicating a similar sensitivity to both cytokines (Fig. 3, bottom). The activity of IL-19, but not those of mda-7 and IL-20, could be detected with 0.1% of supernatant, in agreement with the higher concentration of IL-19 supernatants. When only IL-20R β was transfected, HT-29 cells showed a better response to mda-7 at nonsaturating dilutions (1% and 0.1% supernatant), indicating that this type of complex is more sensitive to mda-7 (Fig. 3 top). Similar results were obtained in HEK293 cells (data not shown).

IL-20R β cannot substitute for IL-10R β in IL-22 signaling

The finding that IL-22R can associate not only with IL-10R β as described previously, but also with IL-20R β raised the possibility that the complex of IL-20R β with IL-22R could mediate an IL-22 response. Because IL-10R β is ubiquitously expressed, we could not address this question by direct transfection, but the role of IL-10R β was assessed with an anti-IL-10R β Ab. As shown in Fig.

4, this Ab could block the IL-22 activity both in control HT-29 cells and in cells transfected with the IL-20R β cDNA, indicating that IL-20R β cannot substitute for IL-10R β when the latter chain is not accessible to IL-22. The same Ab did not affect the activity of mda-7 or IL-20 in the same cells (data not shown).

mda-7, IL-19, and IL-20 do not bind IL-22BP

IL-22BP has been shown to bind IL-22 (12, 13), but nothing is known concerning its ability to bind other IL-10 homologs. The fact that this soluble receptor exhibits the same degree of homology with the extracellular domains of IL-22R and IL-20R α prompted us to test the hypothesis that IL-22BP could also bind IL-20. In a first set of experiments, we tested the ability of the IL-10 homologs to compete for the binding of IL-22BP to insolubilized IL-22. Microtiter plates were coated with rIL-22 and incubated with an IL-22BP-Ig fusion protein in the presence of IL-10 homologs. The interaction between IL-22 and IL-22BP was detected with an anti-Ig Ab. As shown in Fig. 5A, only IL-22 supernatants were able to block IL-22BP binding. To directly assay the

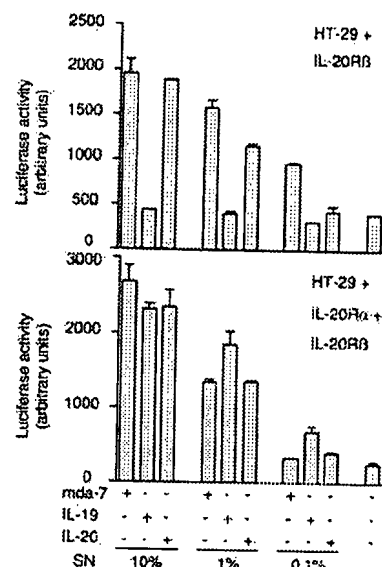


FIGURE 3. Comparison of IL-20 and mda-7 sensitivity with both types of IL-20R complexes. HT-29 cells were transfected with the pGRR5 luciferase construct and the cDNAs encoding IL-20R β alone (top), or IL-20R α and IL-20R β (bottom). Cells were stimulated with different dilutions of mda-7, IL-19, and IL-20 supernatants for 2 h before measuring luciferase activity.

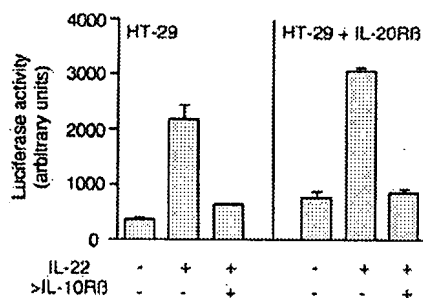


FIGURE 4. IL-20R β cannot substitute for IL-10R β in IL-22 signaling. HT-29 cells were transfected with the pGRR5 luciferase construct and the IL-20R α cDNA. Cells were preincubated 1 h with anti-IL-10R β Ab before stimulation with 10% supernatant from IL-22- or mock-transfected HEK293. Luciferase activity was monitored 2 h later.

interaction between IL-10 homologs and IL-22BP, we coated microtiter plates with anti-flag Ab before incubation with flag-tagged IL-10 homologs. IL-22BP-Ig was added, and interaction was checked with an anti-Ig Ab. As shown in Fig. 5B, only IL-22 was able to bind IL-22BP-Ig, and no other IL-10 homolog showed the same activity.

Discussion

Sharing receptor subunits is a well-known feature within class I cytokine receptors and has allowed to define subfamilies based on the involvement of subunits such as βc , gp130, and IL-2R γ . Among the class II cytokine receptors, the only example of a shared receptor so far was the IL-10R β chain, which is involved in both IL-10 and IL-22 signaling (9–11). In this paper, we show that IL-22R and DIRS1/IL-20R β are also shared by different receptor

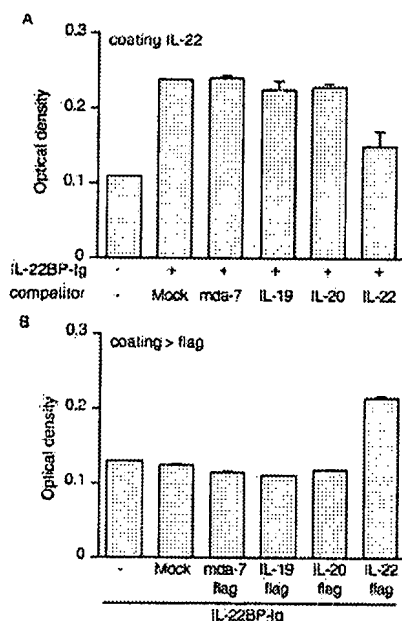


FIGURE 5. IL-22BP interacts specifically with IL-22. *A*, Plates were coated with rIL-22 before addition of IL-22BP-Ig preincubated with IL-10 homologs. Specific interactions were detected with rabbit polyclonal anti-Ig Abs. *B*, Plates were coated with anti-flag Ab. Supernatants containing flag-tagged IL-10 homologs were added before incubation with IL-22BP-Ig. Specific interactions were detected with a rabbit polyclonal anti-mouse Ig.

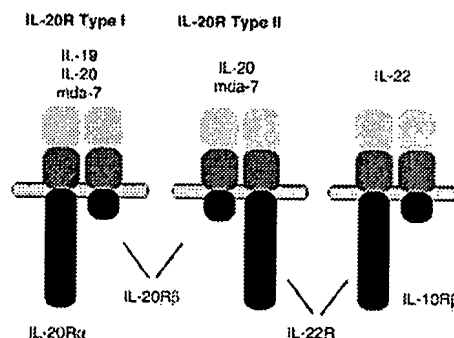


FIGURE 6. Schematic representation of IL-22R and IL-20R complexes.

complexes. The IL-20R β subunit can associate either with IL-20R α , leading to a functional receptor for IL-19, IL-20, and mda-7 (type I IL-20R complex). IL-20R β also can associate with the IL-22R subunit and lead to a functional receptor for IL-20 and mda-7, but not for IL-19 (type II IL-20R complex), as schematically represented in Fig. 6. Additional experiments are needed to determine which of these chains serve as an actual ligand binding component or as a Jak-recruiting subunit. Alternatively, these receptor subunits may be expressed as preassociated complexes at the surface of the cells.

IL-20-transgenic mice show neonatal lethality and skin abnormalities, including thickened epidermis and expression of markers of hyperproliferation (6). Our observations strongly suggest that IL-19 and mda-7 can have a similar activity. Interestingly, IL-19 acts only on type I IL-20R and should therefore recapitulate only partly IL-20 activities. By contrast, IL-20 and mda-7 seem to behave similarly regarding both complexes. Noticeably, expression of the rat ortholog of mda-7 seems to be up-regulated during wound healing, a process that definitely involves keratinocyte proliferation (15).

Although mda-7 was originally identified several years ago (2), its activities and mode of action remain poorly understood. This protein was reportedly expressed intracellularly and was shown to induce apoptosis in certain tumor cell lines by an unknown mechanism (16, 17). On transfection of the mda-7 cDNA in HEK293 cells, we found most of the protein in the supernatant, indicating that it can be secreted, at least in this cell type. Secretion of the rat and mouse orthologs of mda-7 in various cell types also has been reported (3, 4). Together with our observation that exogenous mda-7 binds to the IL-20R complexes, these data support the hypothesis that mda-7 acts as a paracrine or autocrine factor. However, it remains possible that mda-7 might be expressed either as a cytoplasmic protein, inducing cell growth inhibition and apoptosis, or as a secreted protein acting on various cell types through IL-20R complexes.

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